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Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

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4 20

Page 11-19

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(FILE 'HCAPLUS' ENTERED AT 08:54:05 ON 03 DEC 1998)
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FILE 'HCAPLUS' ENTERED AT 09:18:02 ON 03 DEC 1998

L1	81 S EFFICACY (L) ASSAY#
L2	104 S (EFFICACY (3A) ASSAY#)/AB
L3	40708 S SCREEN###
L4	218555 S CHEMOTHERAP? OR CHEMO (L) THERAP? OR DRUG#
L5	3410 S L3 (L) L4
L6	3513 S L2 OR L5
L7	81485 S (CELL# OR TISSUE#) (L) CULTUR?
L8	160 S L7 AND L5
L9	271581 S TUMOR# OR CANCER# OR NEOPLAS?
L10	76 S L9 AND L8
	E L4 (L) EVALUAT?
L11	4597 S L4 (L) EVALUAT?
L12	7928 S L11 OR L6
L13	253 S L12 AND L7
L14	103 S L13 AND L9
L15	58 S TERASAKI OR TERASAKI/AB
L16	1 S L14 AND L15
L17	362744 S APP# OR APPARATUS OR MICROWELL# OR WELL# OR MICROTITER?
L18	4 S L14 AND L17
L19	1 S MULTICELLULAR PARTICULATE#
L20	1 S MULTICELLULAR PARTICULATE#/AB
L21	1 S (MULTICELLULAR PARTICULATE#)/AB
L22	1 S L19 OR L21
L23	1 S L22 AND L12
L24	4 S L16 OR L18 OR L23
L25	6219 S WOUND HEAL?
L26	47 S L25 (L) (L3 OR L2 OR L1 OR EVALUAT?)
L27	5 S L26 AND L7
L28	8 S L27 OR L24

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L28 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1998:268378 HCAPLUS
DN 128:290644
TI Anti-fibrotic agent assay using TGF.beta.1 production by
LPS-stimulated macrophages
IN Jeffrey, C. Geesin; Gosiewska, Anna
PA Johnson & Johnson Medical, Inc., USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
PI WO 9817304 A1 19980430
DS W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ,
VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB,
GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG

AI WO 97-US19451 19971024
 PRAI US 96-29632 19961025
 DT Patent
 LA English
 AB A novel method has been developed for screening anti-scarring and anti-fibrotic agents. This method offers simplicity, it is reproducible and could be adopted to screen a large no. of new potential anti-fibrotic agents. This method has characteristics in common with the BAEC/BASMC co-culture system, but is more sensitive and does not require screening a large no. of clonal lines for developing an effective method. In this system, similarly to the co-culture system, activation of L-TGF-.beta.1 occurs by several independent mechanisms which involve binding of the latent complex to M6P/IGF-II receptors, thrombospondin and/or tissue type II transglutaminase. But, in contrast to the co-culture system, this macrophage-dependent system does not appear to involve plasmin. Using this method, potential novel anti-fibrotic agents such as IGF-II (used sep. or in combination with IGFBP-2 as a delivery vehicle), tissue type II transglutaminase inhibitors and anti-inflammatory agents (such as hydrocortisone) were identified. A potential novel mechanism of action for mannose 6-phosphate has been proposed which is based on downregulation of M6P/IGF-II receptor and TGF-.beta.1 mRNAs.

IC ICM A61K038-16
 ICS A61K038-30; C07K005-00

CC 2-1 (Mammalian Hormones)

IT Drug screening
 Fibrosis
 Granulation tissue
 Peritoneal macrophage
 Wound healing promoters
 (assay for **screening** anti-fibrotic and antiscarring agents using TGF.beta.1 prodn. by LPS-stimulated macrophages)

IT Fetus
 Fibroblast
 (method of identifying modulators of TGF-.beta.1 action in LPS-stimulated macrophages with conditioned **cell culture** medium from fetal fibroblasts)

IT Transforming growth factor .beta.1
 RL: BPR (Biological process); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (method of identifying modulators of TGF-.beta.1 action in LPS-stimulated macrophages with conditioned **cell culture** medium from fetal fibroblasts)

L28 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 1998 ACS
 AN 1998:71095 HCAPLUS
 DN 128:97698
 TI Precise efficacy assay methods for active agents, including chemotherapeutic agents, using cohesive **multicellular particulates**
 IN Kornblith, Paul L.
 PA Precision Therapeutics, Inc., USA
 SO PCT Int. Appl., 16 pp.
 CODEN: PIXXD2
 PI WO 9802038 A1 19980122
 DS W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,

CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, HU, IL, IS,
 JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
 MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL,
 TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD,
 RU, TJ, TM
 RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB,
 GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG

AI WO 97-US11595 19970710
 PRAI US 96-679056 19960712
 DT Patent
 LA English
 AB An improved system is disclosed for screening a multiple of
 candidate therapeutic or chemotherapeutic agents for efficacy as to
 a specific patient, in which a tissue sample from the patient is
 harvested, cultured and sep. exposed to a plurality of treatments
 and/or therapeutic agents for the purpose of objectively identifying
 the best treatment or agent for the particular patient. Specific
 method innovations such as tissue sample prepn. techniques render
 this method practically as well as theor. useful. One particularly
 important tissue sample prepn. technique is the initial prepn. of
 cohesive **multicellular particulates** of the
 tissue sample, rather than enzymically dissocd. cell suspensions or
 preps., for initial tissue culture monolayer prepn. By subjecting
 uniform samples of cells to a wide variety of active agents (and
 concns. thereof), the most promising agent and concn. for treatment
 of a particular patient can be detd.

IC ICM A01N001-02
 ICS C12N001-02; C12N005-00; C12Q001-02; C12Q001-18; C12Q001-24
 CC 1-1 (Pharmacology)
 ST **drug screening tissue culture**
; chemotherapeutic screening tissue
culture
 IT **Apparatus**
 (Terasaki dispenser; precise efficacy assay methods for
 active agents, including chemotherapeutic agents, using cohesive
multicellular particulates)
 IT Radiotherapy
 (agents for; precise efficacy assay methods for active agents,
 including chemotherapeutic agents, using cohesive
multicellular particulates)
 IT Body fluid
 (effusion; precise efficacy assay methods for active agents,
 including chemotherapeutic agents, using cohesive
multicellular particulates)
 IT Animal cells
 Animal tissue
 Antitumor agents
 Ascites
 Chemotherapy
 Cytotoxic agents
Drug screening
 Drugs
 Immunotherapy
 Radioprotectants
 Radiosensitizers (biological)
Tissue culture (animal)
Wound healing promoters

(precise efficacy assay methods for active agents, including chemotherapeutic agents, using cohesive multicellular particulates)

IT Tumors (animal)
(tissue; precise efficacy assay methods for active agents, including chemotherapeutic agents, using cohesive multicellular particulates)

L28 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1997:579741 HCAPLUS
DN 127:229674
TI Methods and compositions related to FKBP12 inhibition of TGF-.beta. receptor-mediated signaling for enhancing cellular response to TGF-.beta. ligands, screening assay, and therapeutic uses
IN Donahoe, Patricia K.; Wang, Tongwen
PA General Hospital Corp., USA
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
PI WO 9731020 A1 19970828
DS W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 97-US2918 19970221
PRAI US 96-12054 19960222
DT Patent
LA English
AB The invention concerns the TGF-.beta. receptor-mediated signaling pathway and is based on the finding that TGF-.beta. receptor-mediated signaling is inhibited by the cytoplasmic interactor FKBP12. The invention further concerns methods and pharmaceutical compns. for enhancing cellular response to TGF-.beta. ligands. A screening assay is also provided for identifying macrolide potentiators capable of binding FKBP12 and thereby blocking FKBP12 inhibition of TGF-.beta. receptor-mediated signaling. Methods are disclosed using the macrolide potentiator and TGF-.beta. ligand for treatment of ulcers, psoriasis, gynecol. tumors, etc.

IC ICM C07K014-52
CC 1-12 (Pharmacology)
Section cross-reference(s): 2

IT Antiulcer agents
Cell proliferation
Connective tissue
Drug delivery systems
Drug screening
Protein sequences
Psoriasis
Second messenger system
Soft tissue
Wound healing promoters
cDNA sequences
(methods and compns. related to FKBP12 inhibition of TGF-.beta. receptor-mediated signaling for enhancing cellular response to TGF-.beta. ligands, screening assay, and therapeutic uses)

IT Tissue culture (animal)
(organ; methods and compns. related to FKBP12 inhibition of

TGF-.beta. receptor-mediated signaling for enhancing cellular response to TGF-.beta. ligands, screening assay, and therapeutic uses)

L28 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 1998 ACS
 AN 1996:359878 HCAPLUS
 DN 125:29580
 TI Electrochemical assessment of cell behavior and metabolic activity
 IN Gearey, David; Woolley, David Edward; Eden, Robert David
 PA University of Manchester Institute of Science and Technology, UK
 SO PCT Int. Appl., 23 pp.
 CODEN: PIXXD2
 PI WO 9610742 A1 19960411
 DS W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM
 RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
 AI WO 95-GB2297 19950929
 PRAI GB 94-19716 19940930
 DT Patent
 LA English
 AB The app. comprises a container into which culture medium has been introduced. Located within the container and partially submerged by the medium is a main electrode, the surface of which is formed by a thin film of gold. This elec. conductive surface supports adherent, variable cells previously grown to near confluence. The container is closed by a lid which is penetrated by a tube filled with an electrochem. conducting medium that is in electrochem. contact with a ref. electrode. The end of the tube is immersed in the culture medium. Another tube is provided through which test factors such as stimulants or suppressants can be injected into the container. The invention enables the provision of an anal. tool for, e.g., the study of specific cell behavior in vitro, such as the effects of drugs, hormones, cytokines, prostaglandins, mutagens, etc. on selected target cells; biocompatibility screening; identification of specific cell types in vivo, e.g., detection of certain tumor cells and their location; selection and optimization of anti-cancer treatment in ex-vivo culture; and assessment of brain activity and regional variations of such activity.
 IC ICM G01N027-416
 ICS C12M001-00
 CC 9-1 (Biochemical Methods)
 Section cross-reference(s): 1, 14
 ST **cell metab electrochem signal detection app;**
culture cell electrochem signal detection
electrode; drug screening cell
culture electrode app; cancer
drug screening electrode app
 IT Animal metabolism
 Animal **tissue culture**
 Electric activity
 Electric circuits
 Electrodes
 Fibroblast
 Mutagens

Neoplasm inhibitors

Neoplasm

Pharmaceuticals

(electrochem. assessment of **cultured cell**

behavior and metab. in relation to **drug**

screening)

IT Hormones

Lymphokines and Cytokines

Prostaglandins

RL: BAC (Biological activity or effector, except adverse); BIOL

(Biological study)

(electrochem. assessment of **cultured cell**

behavior and metab. in relation to **drug**

screening)

IT Medical goods

(antithrombogenic, electrochem. assessment of **cultured**

cell behavior and metab. in relation to **drug**

screening)

IT Mammary gland

(**neoplasm**, carcinoma, electrochem. assessment of

cultured cell behavior and metab. in relation

to **drug screening**)

IT 7440-57-5, Gold, analysis

RL: ARU (Analytical role, unclassified); DEV (Device component use);

ANST (Analytical study); USES (Uses)

(electrochem. assessment of **cultured cell**

behavior and metab. in relation to **drug**

screening)

L28 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 1998 ACS

AN 1992:3217 HCAPLUS

DN 116:3217

TI An electronic technique and **apparatus** of identifying an effective drug for treating a **cancer** patient

IN Malin, Patricia J.

PA Oncotherapeutics, USA

SO PCT Int. Appl., 35 pp.

CODEN: PIXXD2

PI WO 9115595 A1 19911017

DS W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU

RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG

AI WO 91-US2320 19910403

PRAI US 90-503791 19900403

DT Patent

LA English

AB Cancerous cells of a patient under treatment are added to a quantity of cell-life-supporting media along with a quantity of an anti-cancer drug that is a candidate for treating the patient. The elec. cond. of the cell is monitored over time in order to det. the effect of the candidate drug to inhibit increases in vol. or no. of the cancerous cells. Data on the effect of the same drug on normal cells of the patient may simultaneously be gathered so that a drug is chosen which will result in reduced side effects on the patient. A computer system is provided for simultaneously monitoring a large no. of media containers, thereby allowing the effects of >1 drug

and/or >1 concn. of a given drug to be detd. at the same time, within a period of a few hours or a couple of days. Diagrams of the app. are included.

IC ICM C12Q001-02
 CC 9-12 (Biochemical Methods)
 ST anticancer **drug screening** cond app;
 neoplasm inhibitor screening cond app
 IT **Apparatus**
 (for antitumor **drug screening** by detn. of
 cond. change in growth media)
 IT Computer application
 (in antitumor **drug screening** by detn. of
 cond. change in growth media, app. in relation to)
 IT Electrodes
 (in app. for antitumor **drug screening**
 by detn. of cond. change in growth media)
 IT Animal **tissue culture**
 (media for, tumor cell growth-related cond.
 change in, in antitumor **drug screening**)
 IT Electric conductivity and conduction
 (of cancer cell media, change of, in antitumor
drug screening)
 IT Neoplasm inhibitors
 (screening of, cond. app. for)
 IT Electric circuits
 (printed, boards, in app. for antitumor **drug**
screening by detn. of cond. change in growth media)

L28 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 1998 ACS

AN 1990:624562 HCAPLUS

DN 113:224562

TI Preparation and use of amyloid precursor protein (APP) in
 screening assays for Alzheimer's disease therapeutics

IN Neve, Rachael L.; Yankner, Bruce A.

PA Children's Medical Center Corp., USA

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

PI WO 9005138 A1 19900517

DS W: JP

RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE

AI WO 89-US5041 19891108

PRAI US 88-268854 19881108

DT Patent

LA English

AB An assay to screen neuronal toxicity antagonists comprises: (1)
 culturing neurons in the presence of a truncated neurotoxic APP,
 produced by recombinant DNA techniques, and candidate compd.; (2)
 evaluating toxicity to the neuronal cells. The neuron could be a
 (1) primary culture cell of hippocampal, neocortical, or dorsal root
 origin; (2) undifferentiated neuroblastoma, embryonal carcinoma, or
 fibroblast tumor cell under differentiating conditions, e.g. in the
 presence of nerve growth factor, fibroblast growth factor, cAMP,
 phorbol ester, or serum depletion; or (3) recombinant APP
 gene-transfected cells. The truncated recombinant APP comprises the
 amyloid polypeptide sequence, and lacks the serine protease
 inhibitor domain. Anal. of the APP's presence in body fluid with
 anti-APP antibody is useful for monitoring the progression of

Alzheimer's disease. Thus, AB1 and AD1, truncated APP nucleotide sequences, were constructed. The AB1 was transfected into PC12 cells, and the conditioned culture medium was used as APP source directly. The APP-contg. medium immunoabsorbed or not with M4, an anti-APP antibody, was added to a hippocampal cell culture. After 66 h, cell neurons were dead if M4-untreated APP-contg. medium was used; cultures treated with immunoabsorbed conditioned medium were alive and similar in appearance to untreated control.

- IC ICM C07H021-04
- ICS C12N015-11; G01N033-48; C12Q001-02; C12N005-00
- CC 1-1 (Pharmacology)
- Section cross-reference(s): 3, 4
- ST amyloid Alzheimer's disease **drug screening**;
recombinant amyloid Alzheimer **drug screening**;
antibody amyloid Alzheimer diagnosis; cytotoxicity nerve amyloid precursor
- IT Nerve, toxic chemical and physical damage
(amyloid precursor protein toxicity to, **drug screening** for Alzheimer's disease in relation to)
- IT Gene and Genetic element, animal
RL: PROC (Process)
(for amyloid precursor protein, expression of, in **drug screening** for Alzheimer's disease)
- IT Amyloids
RL: BIOL (Biological study)
(precursor protein of, recombinant, neurotoxicity of, **drug screening** for Alzheimer's disease in relation to)
- IT Glycoproteins, specific or class
RL: BIOL (Biological study)
(amyloid A4, pre-, prodn. of recombinant and detection of, in **drug screening** for and diagnosis of Alzheimer's disease)
- IT Carcinoma
(embryonal, differentiation of, amyloid precursor protein effect on, in **drug screening** for Alzheimer's disease)
- IT Brain
(hippocampus, primary **culture cells** from, amyloid precursor protein toxicity to, in **drug screening** for Alzheimer's disease)
- IT Brain
(neocortex, primary **culture cells** from, amyloid precursor protein toxicity to, in **drug screening** for Alzheimer's disease)
- IT Toxins
RL: BIOL (Biological study)
(neuro-, amyloid precursor proteins as, in **drug screening** for Alzheimer disease)
- IT Nerve, **neoplasm**
(neuroblastoma, differentiation of, amyloid precursor protein effect on, in **drug screening** for Alzheimer's disease)
- IT Nerve center and Ganglion
(spinal, primary **culture cells** from, amyloid precursor protein toxicity to, in **drug screening** for Alzheimer's disease)

- IT 130588-75-9, Deoxyribonucleic acid (human clone 9-110
591-653-amyloid A4 glycoprotein precursor-specifying) 130588-76-0
RL: PROC (Process)
(expression of, in amyloid precursor protein prodn. for
drug screening for Alzheimer's disease)
- L28 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1989:33253 HCAPLUS
DN 110:33253
TI The development of **tissue culture** methods for
the in vitro evaluation of polysaccharide wound management products
AU Spyratou, Olga
CS Univ. Wales, UK
SO (1987) 237 pp. Avail.: Univ. Microfilms Int., Order No. BRDX81788
From: Diss. Abstr. Int. B 1988, 49(4), 1108
DT Dissertation
LA English
AB Unavailable
CC 1-1 (Pharmacology)
ST polysaccharide wound healing **tissue culture**
method
IT **Wound healing**
(polysaccharides for, **tissue culture**
screening of, of humans and lab. animals)
IT Polysaccharides, biological studies
RL: BIOL (Biological study)
(wound healing from, **tissue**
culture screening for, of humans and lab.
animals)
IT Animal **tissue culture**
(wound healing polysaccharides
screening by, of humans and lab. animals)
- L28 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 1998 ACS
AN 1984:202991 HCAPLUS
DN 100:202991
TI Use of fibroblast **cell culture** for the study of
wound healing drugs
AU Adolphe, M.; Pointet, Y.; Ronot, X.; Wepierre, J.
CS Inst. Biomed. Cordeliers, Ec. Prat. Hautes Etud., Paris, 75006, Fr.
SO Int. J. Cosmet. Sci. (1984), 6(1), 55-8
CODEN: IJCMDW; ISSN: 0142-5463
DT Journal
LA English
AB In order to study the action of wound healing drugs on the growth of
fibroblasts, they were cultured in a medium contg. a suboptimal
concn. of serum. Several growth factors (eye-derived growth factor
and fibroblast growth factor) were compared with various healing
products for their effects on the growth curve. Some products
slightly increased the proliferation of fibroblasts, in comparison
with the optimal growth obtained with growth factors.
CC 1-1 (Pharmacology)
IT Fibroblast
(**cell culture**, for wound
healing drugs evaluation)
IT **Wound healing**
(drugs for, evaluation of, fibroblast cell

culture for)
IT Animal tissue culture
 (of fibroblasts, for wound healing drugs
 evaluation)

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DERWENT WEEK FOR CHEMICAL CODING: 199842
DERWENT WEEK FOR POLYMER INDEXING: 199844
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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 DEL HIS Y
L1 9 S EFFICACY (3A) ASSAY#
L2 1277 S (CHEMOTHERAP? OR CHEMO THERAP? OR DRUG#) (4A) (SCREEN?
L3 12442 S (CELL# OR TISSUE#) (4A) CULTUR?
L4 1286 S L1 OR L2
L5 1 S (MULTICELLULAR OR MULTI CELLULAR) (3A) PARTICULAT?
L6 0 S L3 AND L4
L7 141 S L3 AND L4
L8 33397 S (CANCER# OR TUMOR# OR TUMOUR# OR NEOPLAS?)
L9 61 S L7 AND L8
L10 1195 S (ASCITES OR EFFUSION)
L11 0 S L9 AND L10
L12 40 S L3 AND L8 AND L10
L13 38662 S (CHEMOTHERAP? OR CHEMO THERAP? OR DRUG# OR WOUND HEAL?)
L14 3 S L12 AND L13
L15 1623 S L3 AND L8
L16 334 S L13 AND L15
L17 2 S L16 AND MONOLAYER?
L18 17175 S MICROTITER# OR MICRO TITER# OR WELLS OR MICROWELL#
L19 3 S L16 AND L18
L20 7 S L19 OR L17 OR L14 OR L5
L21 17525 S L8 AND L13 OR L3
L22 334 S L8 AND L13 AND L3
L23 3 S L22 AND L10
L24 7 S L23 OR L20

FILE 'WPIDS' ENTERED AT 09:40:25 ON 03 DEC 1998

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AN 98-110245 [10] WPIDS
DNC C98-036204
TI Assessing chemo-sensitivity of patient cells using mono-layers grown from **multicellular particulates** - providing samples that relate better to in vivo behaviour, particularly used to select best agents for treating **tumours** in individual patients.
DC B04 D16
IN KORNBLITH, P L
PA (PREC-N) PRECISION THERAPEUTICS INC
CYC 78
PI WO 9802038 A1 980122 (9810)* EN 15 pp
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL
OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI
GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD
MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT UA UG UZ VN YU ZW
US 5728541 A 980317 (9818) 5 pp
AU 9736493 A 980209 (9823)
ADT WO 9802038 A1 WO 97-US11595 970710; US 5728541 A US 96-679056
960712; AU 9736493 A AU 97-36493 970710
FDT AU 9736493 A Based on WO 9802038
PRAI US 96-679056 960712
AB WO 9802038 A UPAB: 980309
Chemosensitivity of patient cells is assessed by:
(a) separating a specimen of tissue, cell **ascites** or **effusion** fluid into **multicellular particulates** (MP);
(b) growing a **tissue culture monolayer** from cohesive MP;
(c) inoculating cells from this layer into many separate sites;
(d) treating the sites with test agents, and
(e) assessing chemosensitivity of the treated cells.
USE - The method is used to identify the best treatment agent and concentration for a particular patient, especially for treatment of **cancer** or other hyper-proliferative diseases such as psoriasis and for **wound healing**. Formation and blocking of enzymes, neurotransmitters and other biologically active compounds can also be screened for.
ADVANTAGE - By using MP, rather than enzyme-dissociated suspensions, to produce a **monolayer**, preparation is simplified and a **cell culture** that retains in vivo reactivity is formed.
Particularly, growth of malignant cells is optimised, without overgrowth of fibroblasts or other cells as often occurs in suspension cultures. The **monolayers** can be grown in a few weeks, contrast longer times required with single cell progeny by dilution cloning.
Dwg.0/0
L24 ANSWER 2 OF 7 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 97-100006 [09] WPIDS
DNC C97-031966
TI Selective potentiation of cell damage - by administering restraining agent to retard progress of cells through cell cycle and targetted cytotoxic insult.

DC B05
 IN GRIMLEY, P M; MEHTA, S
 PA (JACK-N) JACKSON FOUND ADVANCEMENT MILITARY MED
 CYC 71
 PI WO 9701344 A2 970116 (9709)* EN 159 pp
 RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA
 PT SD SE SZ UG
 W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE
 HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW
 MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
 AU 9663960 A 970130 (9720)
 WO 9701344 A3 970327 (9729)
 EP 835111 A2 980415 (9819) EN
 R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
 ADT WO 9701344 A2 WO 96-US10921 960626; AU 9663960 A AU 96-63960 960626;
 WO 9701344 A3 WO 96-US10921 960626; EP 835111 A2 EP 96-923453
 960626, WO 96-US10921 960626
 FDT AU 9663960 A Based on WO 9701344; EP 835111 A2 Based on WO 9701344
 PRAI US 96-668932 960624; US 95-546 950627
 AB WO 9701344 A UPAB: 970320

Method of potentiating cell damage comprises:

(a) administering a restraining agent (RA) to a target cell population to be damaged at a concn. and under conditions sufficient to retard but not arrest the progress of the target cells through the cell cycle, and

(b) applying a targeted cytotoxic insult (TCI) concomitant with or subsequent to the application of the RA.

Also claimed are:

(1) a method of treating a patient suffering from **cancer** or infection, comprising:

(a') delivering a first agent capable of acting as a TCI at high concn. and acting as a RA at low concn. to the patient under conditions sufficient to damage target **cancer** or infected cells,

(b') permitting the concn. of the first target agent to drop to levels where the first agent acts as a RA and

(c') delivering a second agent under conditions sufficient to damage target **cancer** cells when the concn. of the first agent is at a level sufficient to retard but not arrest the progress of the target cells through the cell cycle;

(2) a method of determining synergism or antagonism between two agents implemented by a data processor, comprising:

(a'') receiving in a spreadsheet database input data from test **wells** contg. two agents in bivariate dilutions and from at least 1 control well contg. no agent and from at least 2 control **wells** contg. only one of each of the two agents, where the data represents quantitation of percent growth inhibition,

(b'') processing the spreadsheet according to predetermined relationships comparing the percent growth inhibition in the test **wells** to a hypothetical percent growth inhibition mathematically derived from data from the control **wells** and

(c'') graphically presenting differences between the data from the test **wells** and the hypothetical data;

(3) a data processing system for determining synergism or antagonism between two agents comprising:

(i) a device for receiving a spreadsheet as in (2) (a''),

(ii) a device, coupled to the receiving device, for processing the spreadsheet as in (2) (b'') and

(iii) a device, coupled to the processing device, for graphically presenting differences between the data as in (2) (c'').

USE - The methods can be used for the treatment of **neoplasms**, for the early destruction of cells infected by viruses or in anti-fungal, anti-parasitic or other anti-microbial therapies. They can also be used in the application of herbicides, insecticides or other pesticides designed for the killing of a complex organism, extermination of pests or selective poisoning of organisms. They can also be used in **chemotherapy** or radiant energy therapies to exterminate **neoplastic** cells in the human body or in tissues removed for auto-transplantation or hetero-transplantation; in immunotherapy or transplantation medicine to control the excessive proliferation of abnormally destructive immuno-cytic clones, such as in graft vs. host reactions; in fertility control including destruction of germ line or conceptus tissues; in medical anti-microbial therapies, systemic use with anti-viral, anti-bacterial or anti-fungal agents; in medical anti-malarial or other anti-parasitic **chemotherapies**; in procedures for preventing in vitro contamination of **cell** or organ **cultures** by microbial infections; in killing of **neoplastic** cells in vitro prior to auto-transplantation of bone marrow; in destruction of non-**neoplastic** but functionally abnormal cell clones, e.g. excessively proliferating immune cells (autoimmune disease) and psoriatic epidermal cells; to guide the synthesis or identification of new classes of agents which can be applied as RA or TCI and to lead to new utilisations of presently available agents and to effect a biochemical organ ablation, e.g. thymectomy or prostatectomy.

ADVANTAGE - Using the method the range of concns. of agents for effective synergistic actions can be relatively broad and the target interval during which the effect of a TCI will be max., need not be rigorously restricted.

Dwg.0/38

L24 ANSWER 3 OF 7 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD

AN 90-132582 [18] WPIDS

DNN N90-102742 DNC C90-058243

TI **Cell culture** system for determining **cell** invasion - useful for studying mechanism of cell invasion and in antitumour **drug** effectiveness studies.

DC B04 D16 J04 S03

IN GEHLSSEN, K R; HENDRIX, M J C

PA (REGC) UNIV CALIFORNIA

CYC 1

PI CA 1266603 A 900313 (9018)*

ADT CA 1266603 A CA 85-488708 850814

PRAI US 84-641797 840817

AB CA 1266603 A UPAB: 930928

Cell culture system (I) for determining **cell** invasion through an immobilised membrane comprises (1) a base plate with a predetermined pattern of **wells**; (2) a top plate with apertures formed in a pattern corresp. to that of the **wells** in the baseplate and (3) means for securing the top plate to the base plate with the apertures and corresp. well aligned to define test receptacles.

The receptacles may be partitioned into upper and lower chambers by placing the membrane between the top plate and base plate.

Method for performing cell invasion assays using (I) comprises (a) filling the wells in the bottom plate with a culture medium; (b) securing the top plate to the base plate, with a test membrane in between, so that the apertures are aligned with the wells and partitioned by the membrane; (c) seeding cells to be assayed into the apertures above the membrane in a medium; and (d) observing whether the cells are capable of invading the membrane.

USE/ADVANTAGE - (I) is useful for performing cell invasion assays for assessing the ability of living cells to penetrate biological or synthetic membranes. The system allows utilisation of a single membrane for a multiplicity of tests and allows samples of the cells which have penetrated the membrane to be taken during the course of the assay. The membrane is typically an amniotic membrane and the cells **tumour** cells of cells suspected of being **neoplastic**. The assays are useful both for studying the mechanism of cell invasion and for determining the **chemotherapeutic** efficacy of **drugs** against individual patient **tumours**. @
1/3@

L24 ANSWER 4 OF 7 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 89-085521 [11] WPIDS
DNN N89-065266 DNC C89-037961
TI New polypeptide fibronectin fragments - useful for promoting cell adhesion, heparin binding and/or neurite extension.
DC A96 B04 D16 D22 P32 P34
IN FURCHT, L T; MCCARTHY, J B; FURCHT, T L; MCCARTHY, B J
PA (MINU) UNIV MINNESOTA; (MINU) MINNESOTA UNIVERSITY
CYC 16
PI WO 8901942 A 890309 (8911)* EN 45 pp
RW: AT BE CH DE FR GB IT LU NL SE
W: AU JP
ZA 8806314 A 890426 (8924)
AU 8823859 A 890331 (8927)
US 4839464 A 890613 (8930) 9 pp
EP 366728 A 900509 (9019)
R: AT BE CH DE FR GB IT LI LU NL SE
JP 03500046 W 910110 (9108)
US 5019646 A 910528 (9124) 15 pp
US 5116368 A 920526 (9224) 10 pp
CA 1305084 C 920714 (9234)
US 5147797 A 920915 (9240) 9 pp
US 5171271 A 921215 (9301) 15 pp
EP 366728 B1 930407 (9314) EN 27 pp
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3880139 G 930513 (9320)
US 5294551 A 940315 (9411) 15 pp
JP 2690767 B2 971217 (9804) 16 pp
ADT WO 8901942 A WO 88-US2913 880824; ZA 8806314 A ZA 88-6314 880825; US 4839464 A US 87-89073 870825; EP 366728 A EP 88-908028 880824; JP 03500046 W JP 88-507449 880824; US 5019646 A US 88-225045 880727; US 5116368 A Div ex US 87-89073 870825, US 89-326279 890321; CA 1305084 C CA 88-574721 880815; US 5147797 A Div ex US 87-89073 870825, Div

ex US 89-326279 890321, US 91-741954 910808; US 5171271 A CIP of US 87-89073 870825, Div ex US 88-225045 880727, US 91-662360 910228; EP 366728 B1 EP 88-908028 880824, WO 88-US2913 880824; DE 3880139 G DE 88-3880139 880824, EP 88-908028 880824, WO 88-US2913 880824; US 5294551 A CIP of US 87-89073 870825, Div ex US 88-225045 880727, Div ex US 91-662360 910228, US 92-942597 920909; JP 2690767 B2 JP 88-507449 880824, WO 88-US2913 880824

FDT US 5116368 A Div ex US 4839464; US 5147797 A Div ex US 4839464; US 5171271 A CIP of US 4839464, Div ex US 5019646; EP 366728 B1 Based on WO 8901942; DE 3880139 G Based on EP 366728, Based on WO 8901942; US 5294551 A CIP of US 4839464, Div ex US 5019646, Div ex US 5171360; JP 2690767 B2 Previous Publ. JP 03500046, Based on WO 8901942

PRAI US 87-89073 870825; US 88-225045 880727

AB WO 8901942 A UPAB: 930923

Polypeptides of formula (I)-(VII) are new: Tyr-Clu-Lys-Pro-Gly-Ser-Pro -Pro-Arg-Glu-Val-Val Pro-Arg-Pro-Arg-Pro-Gly-Val. (I); Lys-Asn-Asn-Gly-Lys-Ser-Glu -Pro-Leu-Ile-Gly-Arg-Lys -Lys-Thr-Asp-Glu-Leu (II); Lys-Asn-Asn-Gly-Lys- Ser-Glu-Pro-Leu-Iy-Arg-Lys-Lys-Thr (III); Leu-Ile-Gly-Arg-Lys-Lys-Thr (IV); Tyr-Arg-Val-Arg-Val-Thr-Pro Lys -Gly-Lys-Thr-Gly -Pro-Met-Lys-Glu (V); Ser-Pro-Pro-Arg-Arg-Ala-Arg-Val-Thr (VI); Trp-Gln-Pro-Arg-Ala-Arg-Ile (VII).

USE - (I)-(VII) are fragments of the 33 kD carboxy-terminal heparin-binding region of fibronectin A chain. They promote neurite extension, promote adhesion and spreading of endothelial and melanoma cells and/or promote adhesion of heparin to synthetic substrates. They may thus be useful for assisting nerve regeneration, promoting wound healing and implant acceptance, promoting cell attachment to culture substrates, inhibiting metastasis of malignant cells and/or binding excess heparin in heparin therapy.

0/11

L24 ANSWER 5 OF 7 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD

AN 88-136370 [20] WPIDS

DNC C88-060879

TI New TAF with **neoplastic** effect on blood vessel - is composed of acidic protein with specific mol. wt..

DC B04 D16

PA (NIPK) NIPPON KAYAKU KK

CYC 1

PI JP 63077899 A 880408 (8820)* 7 pp

ADT JP 63077899 A JP 86-217918 860918

PRAI JP 86-217918 860918

AB JP63077899 A UPAB: 930923

TAF is composed of acidic protein having m.w. 30,000-45,000 by gel filtration chromatography, and i.p. 4.5-6.5.

USE/ADVANTAGE - The TAF has **neoplastic** effect of blood vessel by CAM or corneal evaluation test, etc. It is expected to be used as diagnostic agent or **drug**.

In an example, chorioepithelioma cell strain (Bewo) 1.5 x 10 power 6 cells are monolayer cultured on 10% neonatal calf serum, penicillin (100 mcg/ml), streptomycin (100 mcg/ml) contained RPMI 1640 medium (18 ml) at 37 deg.C, under 5% CO2. Medium is exchanged every 1-2 days, and cultured until it reaches to 70-80% confluent. Next, the medium is removed, washed by

Dulbecco's phosphate buffer 3 times, then lactic acid Ringer's soln. (18ml), shaken at 4 deg.C for 4 hours, and TAF secreted conditioned medium (18 ml) is obtained. This conditioned medium (1900 ml) is concd. by Amicon YM-5, and substd. by 5 mM phosphate buffer (pH 7.5). The activity per 1 ml of conditioned medium by Corneal method is 10.4 U. The titre per protein (A280) is 131.2 U/A280. This is treated by DEAE-Toyopearl column chromatography, and next, by treated by DEAE-Toyopearl column chromatography, and next, by molecular sieve chromatography. From the fractionated and purified fraction, the fraction (No. 7) that contains 32% of the total activity, and relative activity of 1230 U/A280 nm is obtained.

0/3

L24 ANSWER 6 OF 7 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
 AN 87-294418 [42] WPIDS
 DNC C87-125019
 TI Anticancer **drug** - contg. hot water extract of pine cone from pinus spp., as active component.
 DC B04
 PA (SAKA-I) SAKAGAMI H
 CYC 1
 PI JP 62205032 A 870909 (8742)* 3 pp
 JP 03042245 B 910626 (9129)
 ADT JP 62205032 A JP 86-47004 860304; JP 03042245 B JP 86-47004 860304
 PRAI JP 86-47004 860304
 AB JP62205032 A UPAB: 930922
 Anticancer **drug** contains hot water extract of pine cone from Pinus parviflora Sieb et Zucc etc., as active ingredient.
 USE/ADVANTAGE - This extract is effective against mice transplanted **ascites tumor** (Meth A fibrosarcoma : BA LB/c mice) (also effective against ddY mice : Sarcoma 180). Also it has differentiating effect against human **cultured** myeloid leukemia **cell** ML-1 to induce macrophage like cells. The toxicity is low. It can be used for anticancer .
 In an example, as pine cone, esp. Pinus parviflora Sieb at Zucc origin, collected in Octobe is pref. For extn, ca. 4-5 hours is needed, until the H2O vol. reduce by 1/2 The hot H2O extract is filtered by gauze, or filter paper, after cooling. To alleviate the bitter taste, correctives e.g. glycyrrhiza may be added. Amt. of H2O for extn is 1.8l against 6 - 7 pine cones. Each half cup of extrant is administered 3 times a day before meals. 100 pine cone (432 g) collected in autumn at Nagasaki city is put into reaction vessel, 5l H2O is added and boiled mildly until the H2O vol. becomes 3 l, for 4 - 5 hours. After cooling, centrifuged at room temp. 10000-xg for 30 min to remove the insol. materials. To the supernatant,, NaCl is added and the osmotic pressure is adjusted to isotonic (290 mOsm). This is filtered by sterilised millipore filter (pore size 0.22 micro-um). It is used for anticancer test.

0/0

L24 ANSWER 7 OF 7 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
 AN 83-05090K [03] WPIDS
 DNN N83-009764 DNC C83-005027
 TI Bifunctional mono clonal antibodies - produced by hybridoma-hybridoma or hybridoma-lymphocyte fusion prods..
 DC B04 D16 S03
 IN READING, C L

PA (TEXA) UNIV TEXAS SYSTEM

CYC 13

PI EP 68763 A 830105 (8303)* EN 27 pp

R: AT BE CH DE FR GB IT LI NL SE

JP 58059994 A 830409 (8320)

US 4474893 A 841002 (8442)

CA 1190873 A 850723 (8534)

EP 68763 B 870408 (8714) EN

R: AT BE CH DE FR GB IT LI NL SE

DE 3276007 G 870514 (8720)

US 4714681 A 871222 (8801)

JP 03067678 B 911023 (9146)

JP 04228067 A 920818 (9240) 11 pp

JP 04228068 A 920818 (9240) 11 pp

EP 68763 B2 930421 (9316) EN 15 pp

R: AT BE CH DE FR GB IT LI NL SE

JP 05065155 B 930917 (9340) 13 pp

JP 08004496 B2 960124 (9608) 12 pp

ADT EP 68763 A EP 82-303197 820618; US 4474893 A US 81-279248 810701; US 4714681 A US 84-621394 840618; JP 03067678 B JP 82-115320 820701; JP 04228067 A Div ex JP 82-115320 820701, JP 91-138041 820701; JP 04228068 A Div ex JP 82-115320 820701, JP 91-138042 820701; EP 68763 B2 EP 82-303197 820618; JP 05065155 B Div ex JP 82-115320 820701, JP 91-138041 820701; JP 08004496 B2 JP 91-138042 910610

FDT JP 05065155 B Based on JP 04228067; JP 08004496 B2 Based on JP 04228068

PRAI US 81-279248 810701; US 84-621394 840618

AB EP 68763 A UPAB: 930925

The following are claimed: (A) an antibody having binding affinity for two different antigens; (B) prodn. of a recombinant monoclonal antibody by incubating a hybrid trioma or quadroma **cell** in **culture** or in the peritoneal cavity of a mouse, and separating soluble protein from the culture supernatant or **ascites** fluid; (C) a trioma or quadroma; (D) a **cell culture** formed by somatic **cell** fusion of two different parental cells characterised in that it is a trioma formed by fusion of a hybridoma and a lymphocyte or a quadroma formed by fusion of two hybridomas.

Potential applications of bifunctional recombinant monoclonal antibodies include analytical and diagnostic techniques, targeted delivery of biological and pharmacological agents to specific cells, and identification and localisation of specific antigens, receptors and cell surface substances.

=> fil biosis

FILE 'BIOSIS' ENTERED AT 10:09:17 ON 03 DEC 1998

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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 18 November 1998 (981118/ED)

CAS REGISTRY NUMBERS (R) LAST ADDED: 18 November 1998 (981118/UP)

=> d his 125-

(FILE 'WPIDS' ENTERED AT 09:40:25 ON 03 DEC 1998)

FILE 'BIOSIS' ENTERED AT 09:41:21 ON 03 DEC 1998

L25 22862 S (CHEMOTHERAP? OR CHEMO THERAP? OR DRUG#) (3A) (EFFICACY
L26 7659 S (CHEMOTHERAP? OR CHEMO THERAP? OR DRUG#) (3A) EVALUAT?
L27 27399 S L25 OR L26
L28 191875 S (TISSUE# OR CELL#) (3A) CULTUR?
L29 452 S L27 AND L28
L30 728910 S TUMOR# OR TUMOUR# OR CANCER# OR NEOPLAS?
L31 173 S L29 AND L30
L32 15 S L31 AND MONOLAYER?
L33 447552 S 24008/CC
L34 439498 S 32500/CC OR 24005/CC
L35 95 S L31 AND L33 AND L34
L36 222 S CHEMOSENSITIVITY (3A) ASSAY
L37 18 S CHEMO SENSITIVITY (3A) ASSAY
L38 6 S EFFICACY ASSAY# AND (CHEMOTHERAP? OR CHEMO THERAP? OR
L39 0 S MULTICELLULAR PARTICULATE?
L40 238 S L36 OR L37
L41 27607 S L27 OR L40
L42 792 S L41 AND L33 AND L34
L43 640 S L30 AND L42
L44 1451664 S (DRUG# OR CHEMOTHERAP? OR CHEMO THERAP? OR CHEMOSENSITI
L45 620 S L43 AND L44
L46 65 S L45 AND CULTUR?/TI,ST
L47 41 S L46 AND (L33) AND 32500/CC AND 24005/CC
L48 2 S L47 AND MONOLAYER#

FILE 'BIOSIS' ENTERED AT 10:09:17 ON 03 DEC 1998

=> d bib ab 147 1-41

L47 ANSWER 1 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 98:349875 BIOSIS
DN 01349875
TI Postconfluent multilayered cell line **cultures** for selective
screening of gemcitabine.
AU Smitskamp-Wilms E; Pinedo H M; Veerman G; Ruiz Van Haperen V W T;
Peters G J
CS Dep. Med. Oncology, Univ. Hosp. VU, P.O. Box 7057, 1007 MB Amsterdam,
Netherlands
SO European Journal of Cancer 34 (6). 1998. 921-926. ISSN: 0959-8049
LA English
AB The in vitro cytotoxicity of gemcitabine (dFdC) was tested in ovarian
and colon **cancer** cell lines grown as monolayers and
three-dimensional multilayered cell cultures. In our model, dFdC
showed slight selectivity in cytotoxicity against ovarian over colon
cancer cells, when cell lines were grown as monolayers.
However, when cell lines were grown as multilayers, this selectivity
was accentuated: A2780 multilayers were 14 times less sensitive than
monolayers, but the colon **cancer** cell lines were more than
1000 times more resistant than their corresponding monolayers. The
accumulation of the active metabolite, dFdCTP, after 24 h exposure to

1 μ -M dFdC varied between 1100 and 1900 pmol/10⁶ cells in monolayers. This was 5 times lower in multilayers compared with monolayers of an four cell lines, which can, in part, explain the lower sensitivity of the multilayers. In addition, it appears that the amount of the active metabolite retained is more important than the amount accumulated initially, since the differences between the ovarian and the colon **cancer** cell lines were more evident in retention experiments. Exposure to dFdC caused a 2-3-fold increase in the levels of several nucleotides, except for the CTP pools in the colon **cancer** lines, which were reduced by 3-fold at the highest dFdC concentration (10 μ -M). The findings with the multilayer model are in better agreement with in vivo activity in ovarian **cancer** and colon **cancer** than those with the monolayer system. This indicates the potential of the multilayer system to be a better predictive model than the conventionally used monolayer cultures.

L47 ANSWER 2 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 97:417623 BIOSIS

DN 99716826

TI High-volume screening.

AU Page M

CS Cancerol. Lab., Dep. Biochem., Univ. Laval Fac. Med., Ste-Foy, PQ, Canada

SO Teicher, B. A. (Ed.). Cancer Drug Discovery and Development, 2. Anticancer drug development guide: Preclinical screening, clinical trials, and approval. xii+311p. Humana Press Inc.: Totowa, New Jersey, USA. 0 (2). 1997. 3-21. ISBN: 0-89603-461-5

DT Book

LA English

L47 ANSWER 3 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 96:391947 BIOSIS

DN 99114303

TI A multilayered postconfluent **tumor cell culture** system for in vitro **drug screening**.

AU Smithskamp-Wilms E; Hendriks H R; Pizao P E; Giaccone G; Pinedo H M; Peters G J

CS EORTC-NDDO, Free Univ. Hosp., Amstelveenseweg 601, 1081 JC Amsterdam, Netherlands

SO Arnold, W., P. Koepf-Maier and B. Micheel (Ed.). Contributions to Oncology, Vol. 51. Immunodeficient animals: Models for cancer research; Workshop on Immunodeficient Laboratory Animals, Berlin, Germany, October 3-6, 1993. xiii+229p. S. Karger AG: Basel, Switzerland; New York, New York, USA. 51 (0). 1996. 204-208. ISBN: 3-8055-6270-5 ISSN: 0250-3220

DT Book; Conference

LA English

L47 ANSWER 4 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 96:383639 BIOSIS

DN 99105995

TI Assay of anticancer **drugs** in tissue **culture**:

Comparison of a tetrazolium-based assay and a protein binding dye assay in short-term **cultures** derived from human malignant glioma.

AU Haselsberger K; Peterson D C; Thomas D G T; Darling J L

CS Neuro-Oncol. Sect., Gough-Cooper Dep. Neurol. Surg., Inst. Neurol.,
Natl. Hosp. Neurol. Neurosurg., Queen Square, London WC1N 3BG, UK
SO Anti-Cancer Drugs 7 (3). 1996. 331-338. ISSN: 0959-4973
LA English
AB Because of the methodological difficulties associated with the MTT
assay in screening short-term cultures derived from human malignant
glioma, a **chemosensitivity assay** based on the
protein staining using sulforhodamine B (SRB) has been optimized for
use with these cells. SRB at a fixed dye concentration achieved
maximal staining density at 20 min for most cell lines and this
intensity was not further increased by using dye concentrations above
0.2%. A delay in staining after fixation did not significantly
decrease staining intensity, but delay in dye extraction after
fixation and staining did. There was an excellent quantitative and
qualitative linear relationship between cell number determined by
either the SRB assay or by cell counting, but not with the MTT assay
which consistently underestimated the number of cells in assay
plates. The MTT assay appeared to be incapable of detecting less than
about 150 cells/well, while these small numbers of cell were readily
detectable by either cell counting or SRB staining. There was a close
correlation between chemosensitivity values derived from the MTT and
SRB assays for procarbazine, CCNU and vincristine when the endpoint
is taken as either the ID-25, ID-50 or ID-75. The results indicate
that the SRB is capable of producing broadly similar results to the
MTT assay, but is more sensitive in the detection of small numbers of
cells with a linear relationship between cell number and SRB staining
intensity over a wide range of cell numbers. It is capable of
producing data from short-term cultures from malignant glioma and
offers technical advantages over the MTT assay in that plates may
safely be stored at certain points during the assay without the need
for immediate processing. The SRB assay provides a useful alternative
to the MTT assay for determining the sensitivity of short-term
cultures of human glioma to cytotoxic drugs.

L47 ANSWER 5 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 95:219475 BIOSIS
DN 98233775
TI A novel bioactive delta lactone FD-211 taxonomy, isolation and
characterization.
AU Nozawa O; Okazaki T; Sakai N; Komurasaki T; Hanada K; Morimoto S;
Chen Z-X; He B-M; Mizoue K
CS Dep. Appl. Biol., Res. Cent. Taisho Pharm. Co. Ltd., 1-403
Yoshino-cho, Omiya-shi, Saitama 330, Japan
SO Journal of Antibiotics (Tokyo) 48 (2). 1995. 113-118. ISSN:
0021-8820
LA English
AB During our screening program for natural product drugs effective
against multidrug-resistant mammalian cells. we have discovered a new
delta lactone FD-211 from the fermentation broth of Myceliophthora
lutea TF-0409. FD-211 had a broad spectrum activity against cultured
tumor cell lines, including adriamycin-resistant HL-60 cells.

L47 ANSWER 6 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 95:146837 BIOSIS
DN 98161137
TI Testing **chemosensitivity** in primary breast **cancers**

- AU Rittmann P; Kochli O R; Schar G; Haller U
CS Gynakol. Klinik, Dep. Frauenheilkunde, Universitaetsspital, Zurich, Switzerland
SO Annual Meeting of the Swiss Society for Gynecology and Obstetrics, Lausanne, Switzerland, June 29-July 2, 1994. Archives of Gynecology and Obstetrics 255 (SUPPL.). 1994. S457. ISSN: 0932-0067
DT Conference
LA German
- L47 ANSWER 7 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 95:23987 BIOSIS
DN 98038287
TI TCA-100 **tumour chemosensitivity assay:**
Differences in sensitivity between **cultured tumour** cell lines and clinical studies.
AU Andreotti P E; Linder D; Hartmann D M; Cree I A; Pazzagli M; Bruckner H W
CS BATLE LE Inc., Fort Lauderdale, FL 33334, USA
SO Journal of Bioluminescence and Chemiluminescence 9 (6). 1994. 373-378. ISSN: 0884-3996
LA English
AB The BATLE LE TCA-100 **tumour chemosensitivity assay** has been used to **evaluate chemotherapeutic drug** sensitivity of cultured **tumour** cell lines. Studies were performed using test drug concentrations calibrated to discriminate sensitivity and resistance of clinical specimens. Strong sensitivity which appeared to be inconsistent with clinical experience was detected for some drugs and cell lines. Findings of strong sensitivity were consistent with basic differences between sensitivity testing cultured cell lines and clinical specimens. Results with cell lines frequently may not apply directly to clinical applications. Characterization of differences between cell lines and clinical specimens may assist in application of cell line findings to clinical trials.
- L47 ANSWER 8 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 93:166224 BIOSIS
DN BA95:87274
TI IN-VITRO PREDICTION OF CYTOSTATIC **DRUG** RESISTANCE IN PRIMARY CELL **CULTURES** OF SOLID MALIGNANT **TUMOURS**.
AU DIETEL M; BALS U; SCHAEFER B; HERZIG I; ARPS H; ZABEL M
CS INST. PATHOL., CHRISTIAN-ALBRECHTS, UNIV. KIEL, MICHAELISSTR. 11, D-2300 KIEL 1, GER.
SO EUR J CANCER 29A (3). 1993. 416-420. CODEN: EJCAEL ISSN: 0959-8049
LA English
AB The in vitro monolayer proliferation assay (MP-assay) described here enables predictive determination of the **efficacy** of anticancer **drugs** considered for clinical application. The assay was designed (1) to achieve a high plating efficiency, (2) to adapt in vitro growth as close as possible to in vivo conditions, and (3) to prove that the cells in vitro correspond with the in vivo **tumour** cells they were derived from. From 452 freshly explanted or biopsied **tumours**, 321 (71%) proliferating cultures could be established. To prove malignant origin of the incubated cells each strain was characterized by DNA-cytophotometry for aneuploidy and by immunocytochemistry for marker proteins. Drug potency was determined by comparing the number of living cells in

drug-treated cultures with non-treated controls. Drug concentrations in vitro corresponded with those achievable in **tumour** tissue and thus represented clinically relevant levels. Growth inhibition in vitro was correlated with in vivo **tumour** response. Two hundred in vitro/in vivo correlations were performed (50 retrospective, 150 prospective). Overall predictive accuracy of the MP-assay was 86%, with correct indication of resistance in 94.5% and of sensitivity in 75.8% ($P < 0.001$). The results show that the proposed assay is capable of estimating the response probability of cytostatic drugs in individual **tumours** and thus can contribute to reducing the applications of non-effective drugs and, within limitations, to improving the basis of drug selection.

L47 ANSWER 9 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 93:143637 BIOSIS

DN BA95:76437

TI STUDIES ON CELL BIOLOGY AND **CHEMOTHERAPY** OF LUNG

CANCER USING TISSUE **CULTURE** TECHNIQUES PART 1.

DRUG SENSITIVITY TEST IN LUNG CANCER USING HUMAN

TUMOR CLONOGENIC ASSAY.

AU KISHIMOTO N

CS SECOND DEP. INTERNAL MED., OKAYAMA UNIV. SCH. MED., OKAYAMA 700, JPN.

SO OKAYAMA IGAKKAI ZASSHI 104 (9-10). 1992. 897-904. CODEN: OIZAAV

ISSN: 0030-1558

LA Japanese

AB The selection of a series of effective drugs for individual patients in advance of drug therapy should increase the success of

cancer chemotherapy. The human **tumor** clonogenic assay was **evaluated** as a **drug** sensitivity test mainly in patients with lung **cancer**. **Tumor** cells from malignant pleural effusion, **tumor**-positive bone marrow aspirates, and **tumor** tissues from the primary or metastases were used as specimens. Prior to plating, **tumor** cells were exposed to 4-hydroperoxy ifosfamide, Adriamycin, mitomycin C, methotrexate, and cisplatin for one hour at graded concentrations which were achievable in man. Of 151 specimens tested, 93 (62%), yielded at least 5 colonies in the control plates containing no drugs. Colony growth (.gtoreq. 5/plate) was seen in 80% of squamous cell carcinoma, in 73% of small cell carcinoma, in 62% of adenocarcinoma, and in 40% of large cell carcinoma. Among the 93 specimens with colony growth, 62 yielded more than 30 colonies in the control plates and were put in force for drug sensitivity testing. Of 37 instances in which the clinical response to a certain drug was examined, 34 (92%) showed an in vitro-in vivo correlation, showing a true positive rate of 57% and a true negative rate of 100%. In summary, the human **tumor** clonogenic assay would be an excellent technique for testing the drug sensitivity of the **tumor** in individual patients **tumor**.

L47 ANSWER 10 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 93:76765 BIOSIS

DN BA95:41265

TI CLONING OF HUMAN **TUMOR** CELL LINES IN POROUS GLASS CAPILLARY

TUBES A FURTHER DEVELOPMENT OF THE HUMAN **TUMOR** STEM CELL

ASSAY.

AU WEISSER H; SCHNABEL R; LANGER P; LATHAN B

CS INST. CLINICAL CHEM., LAB. MED., UNIV. CLIN. BERGMANNSSHEIL,

GILSINGSTRASSE 14, D 4630 BOCHUM 1, GER.

SO INT J CELL CLONING 10 (6). 1992. 352-358. CODEN: IJCCE3 ISSN: 0737-1454

LA English

AB The conventional human **tumor** stem cell assay for cloning **tumor** cells for drug sensitivity testing is limited by its inability to test drug combinations. In an attempt to overcome this limitation, we cloned **tumor** cell lines within porous glass capillary tubes. In contrast to plastic porous tubes, the porous glass membranes were transparent, and colony formation could be judged on an inverted microscope. Human as well as animal cell lines showed sufficient colony growth. Colonies formed within these porous tubes were homogeneously distributed, and their morphology was similar to those formed in the common stem cell assay. Cloning efficiency and colony size depended on the mean pore diameter of the glass membrane, with test colony growth within tubes with a pore diameter ranging from 8.5 nm to 14 nm. A linear relationship between number of cells seeded and number of grown colonies could be demonstrated for the cell lines MDA-231 and Colo 201. Colony growth achieved within porous glass capillary tubes is comparable to that achieved in Petri dishes and in nonporous tubes. We conclude that the porous capillary cloning system meets the basic suppositions for a quantitative cloning assay. Moreover, the porosity of the glass membrane offers the possibility of variable perfusion of medium and drugs. Further investigations will focus on various perfusion modalities and chemosensitivity testing.

L47 ANSWER 11 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 91:274462 BIOSIS

DN BA92:7077

TI IN-VITRO MODEL FOR INTRINSIC DRUG RESISTANCE EFFECTS OF PROTEIN KINASE C ACTIVATORS ON THE CHEMOSENSITIVITY OF CULTURED HUMAN COLON CANCER CELLS.

AU DONG Z; WARD N E; FAN D; GUPTA K P; O'BRIAN C A

CS DEP. CELL BIOL., M. D. ANDERSON CANCER CENT., 1515 HOLCOMBE BLVD., BOX 173, HOUSTON, TEXAS 77030.

SO MOL PHARMACOL 39 (4). 1991. 563-569. CODEN: MOPMA3 ISSN: 0026-895X

LA English

AB We investigated the effects that phorbol ester and diacylglycerol protein kinase C (PKC) activators had on the chemosensitivity of the human colon **cancer** cell line KM12L4a to Adriamycin (ADR), vincristine (VCR), and vinblastine (VLB) and on the intracellular accumulation of those drugs. Exposure of the cells to the PKC activator phorbol-12,13-dibutyrate (PDBu) (15 nM) during a 96-hr in vitro **chemosensitivity assay** significantly reduced the sensitivity of KM12L4a cells to ADR, VCR, and VLB, but not to 5-fluorouracil. Because a 96-hr treatment with 15 nM PDBu did not down-regulate PKC activity in KM12L4a cells, activation of PKC appeared to be responsible for the observed protection conferred by PDBu. PDBu-induced alterations in drug accumulation may account for its protective effects against these cytotoxic drugs, because both PDBu and the phorbol ester 12-O-tetradecanoylphorbol-13-acetate significantly reduced accumulation of [3H]VCR and [14C]ADR in the cultured human colon **cancer** cells. Unsaturated diacylglycerols are structural and functional analogues of phorbol ester PKC activators that are present in the lumen of the colon. We found that treatment of KM12L4a human colon **cancer** cells

with the diacylglycerol 1-oleoyl-2-acetyl-sn-glycerol (OAG) significantly reduced [14C]ADR and [3H]VCR accumulation in the cells. The effects of OAG were dose dependent at physiological diacylglycerol concentrations and were completely reversed by the protein kinase inhibitors H7. OAG, which is rapidly metabolized in cultured cells, and did not protect KM12L4a cells against the cytotoxic drugs in our 96-hr in vitro **chemosensitivity assay**. However, rapid metabolism of diacylglycerols should not limit their capacity to activate PKC in the colonic epithelium in vivo, because that tissue is chronically exposed to replenished supplies of unsaturated diacylglycerols in the intestinal tract. Our results provide evidence that unsaturated diacylglycerols may be environmental factors that contribute to the intrinsic drug resistance of colon **cancer** in vivo by reducing drug accumulation in the carrier cells.

L47 ANSWER 12 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
 AN 91:229457 BIOSIS
 DN BA91:120917
 TI AN EFFICIENT METHOD FOR **CULTURING** HUMAN BREAST CARCINOMA TO **EVALUATE** ANTIBLASTIC DRUG ACTIVITY IN-VITRO EXPERIENCE ON 136 PRIMARY **CANCERS** AND ON 116 RECURRENCES.
 AU ZOLI W; VOLPI A; BONAGURI C; RICCOBON A; SAVINI S; BRIZIO R; SARAGONI A; MEDRI L; MARRA G A; AMADORI D
 CS ONCOLOGICAL DEP., MORGAGNI-PIERANTONI HOSPITAL, U.S.L. 38, VIALE FORLANINI, 47100 FORLI, ITALY.
 SO BREAST CANCER RES TREAT 17 (3). 1991. 231-238. CODEN: BCTRD6 ISSN: 0167-6806
 LA English
 AB The feasibility of techniques developed for isolating and culturing human mammary epithelial cells of malignant origin was confirmed in 136 primary breast **cancers**, 116 hypodermal metastases, and 8 metastatic lymph nodes. In 115 (84%) primary breast **cancers** and in 81 (70%) hypodermal recurrences we observed a good in vitro cellular proliferation. These proliferating cells, at the second passage, were used for a clonal assay suitable for quantitating drug sensitivity. With this clonal assay median cloning efficiencies of 14% and 6% were obtained respectively in primaries and in skin recurrences. We examined the in vitro response to different drugs and confirmed the test's ability to detect heterogeneity in response to same drugs (doxorubicin, 4'-epidoxorubicin, vinblastine, cis platinum, and idarubicinol) among the different breast carcinoma cultures as well as heterogeneity among subpopulations within a single carcinoma.

L47 ANSWER 13 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
 AN 91:183021 BIOSIS
 DN BA91:97770
 TI MORPHOMETRIC AND COLORIMETRIC ANALYSIS OF HUMAN **TUMOR** CELL LINE GROWTH AND **DRUG** SENSITIVITY IN SOFT AGAR **CULTURE**.
 AU ALLEY M C; PACULA-COX C M; HURSEY M L; RUBINSTEIN L R; BOYD M R
 CS LAB. DRUG DISCOVERY RES. AND DEV., DEV. THERAPEUTICS PROGRAM, DIV. CANCER TREATMENT, NATL. CANCER INST., FREDERICK CANCER RES. AND DEV. CENT., FREDERICK, MD. 21701-1013.
 SO CANCER RES 51 (4). 1991. 1247-1256. CODEN: CNREA8 ISSN: 0008-5472
 LA English

AB Previous studies have demonstrated the suitability of image analysis of tetrazolium-stained colonies to assess growth and drug sensitivity of human **tumor** cells cultivated in soft agar culture. In the present study, the potential utility of colorimetric analysis to expedite experimental **drug evaluations** using human **tumor** cell lines was investigated. The same culture dishes were assessed by image analysis and by formazan colorimetry for purposes of comparing multiple methods of measuring growth as well as growth inhibition. Replicate cultures treated with 2-(p-iodonitrophenyl)-3-p-nitrophenyl-5-phenyltetrazolium chloride or 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide exhibited nearly identical colony and volume indices as well as excellent correlation in colorimetric end points. Colony-forming unit volume analysis versus colorimetric assessment of the same cultures following dimethylsulfoxide extraction of protamine sulfate-rinsed, dried soft agar cultures exhibited excellent linear correlation for both growth (Pearson ranging from 0.95 to 1.00) and drug sensitivity (Pearson r ranging from 0.90 to 0.99, and Spearman r ranging from 0.82 to 0.97) and similar drug sensitivity profiles. Results of the current investigation indicate that end points of soft agar culture remain stable for a period of at least 2 weeks following assay termination. In addition, a colorimetric detection range of 1.3-2.2 log units permits determinations of survival levels ranging from 100 to 5% of respective control levels. Colorimetric analysis is anticipated to expedite soft agar colony formation assay evaluations (a) by reducing the need to use the more rigorous and time-consuming image analysis procedures to measure activity in preliminary drug sensitivity assays and (b) by permitting the determination of effective concentration ranges of new experimental agents for subsequent, more detailed investigations.

L47 ANSWER 14 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 90:134502 BIOSIS

DN BA89:73313

TI ADRIAMYCIN RESPONSE OF TWO HUMAN **TUMOR** XENOGRAFTS USING A DOUBLE-RADIOLABEL ORGAN **CULTURE** METHOD.

AU SULLIVAN J L; SULLIVAN L G

CS DEP. PATHOL., MED. UNIV. SOUTH CAROLINA, CHARLESTON, S.C. 29425, USA.

SO NEOPLASMA (BRATISL) 36 (6). 1989. 685-690. CODEN: NEOLA4 ISSN: 0028-2685

LA English

AB A double-radiolabel method of quantitating drug response in a simple organ culture system was used to study the effects of adriamycin on two human **tumor** xenografts in vitro. Explants of X56, an adenocarcinoma of colon, and HXG2, an amelanotic melanoma, both maintained by serial transplantation in athymic mice, were sequentially incubated in vitro with 14C-thymidine, one of several concentrations of adriamycin, and then 3H-thymidine. The ratios of second to first radiolabel incorporation declined as a function of adriamycin concentration. HXG2 was significantly more responsive to adriamycin than X56 in the double-radiolabeled assay. Greater sensitivity of HXG2 was confirmed by three additional methods: The human **tumor** stem cell assay (HTSCA), chemotherapy trials in **tumor**-bearing athymic mice, and a double-radiolabel protocol in vivo in **tumor**-bearing athymic mice. An organ culture method of this type may be useful in screening individual patients' **tumors** for drug resistance.

- L47 ANSWER 15 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 90:71819 BIOSIS
DN BA89:39645
TI IN-VITRO SENSITIVITY TESTING OF MALIGNANT **TUMORS** CLINICAL RESULTS WITH THE ORGAN **CULTURE**.
AU EBERT A; LENK H; GEYER J; TANNEBERGER S
CS ZENTRALINST. KREBSFORSCHUNG DER ADW DER DDR, LINDENBERGER WEG 80, BERLIN, DDR-1115.
SO ARCH GESCHWULSTFORSCH 59 (6). 1989. 455-461. CODEN: ARGEAR ISSN: 0003-911X
LA German
AB An organ culture **assay** for in vitro **chemosensitivity** testing was used to predict clinical responses of various **tumors** to antineoplastic chemotherapy. 9 patients with advanced mammary carcinomas, 7 patients with metastatic malignant melanomas, 1 patient with advanced ovarian **cancer**, 1 with bronchiogenic carcinoma, 1 with metastatic leiomyosarcoma and 1 patient with a metastatic carcinoma of the seat gland were included in the study. 20 in vitro-in vivo correlations were evaluable. 5/9 of the mammary carcinomas showed an objective response, 0/7 malignant melanomas were sensitive in vivo. Further investigations have to assess the value of chemosensitivity assays to predict clinical response for patients with solid **tumors**.
- L47 ANSWER 16 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 89:397850 BIOSIS
DN BR37:64498
TI IMPLEMENTATION OF A PILOT-SCALE HIGH FLUX ANTICANCER **DRUG SCREEN** UTILIZING DISEASE-ORIENTED PANELS OF HUMAN **TUMOR CELL LINES IN CULTURE**.
AU MONKS A; SCUDIERO D; SKEHAN P; BOYD M
CS PRI, DTP, NCI-FCRF, FREDERICK, MD. 21701, USA.
SO EIGHTIETH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, SAN FRANCISCO, CALIFORNIA, USA, MAY 24-27, 1989. PROC AM ASSOC CANCER RES ANNU MEET 30 (0). 1989. 607. CODEN: PAMREA
DT Conference
LA English
- L47 ANSWER 17 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 89:397846 BIOSIS
DN BR37:64494
TI ENRICHMENT OF **TUMOR STEM CELLS** BY SHORT TERM HIGH DENSITY STHD INCUBATION IN THE ADHESIVE **TUMOR CELL CULTURE** SYSTEM ATCCS IMPLICATIONS FOR **DRUG SCREENING**.
AU BAKER F L; SPITZER G; AJANI J A; BROCK W A; SANGER J L; WIKE J
CS UNIV. TEX. M.D. ANDERSON CANCER CENT., HOUSTON, TEX. 77030, USA.
SO EIGHTIETH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, SAN FRANCISCO, CALIFORNIA, USA, MAY 24-27, 1989. PROC AM ASSOC CANCER RES ANNU MEET 30 (0). 1989. 606. CODEN: PAMREA
DT Conference
LA English
- L47 ANSWER 18 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 89:247077 BIOSIS
DN BA87:128142
TI ACTIONS OF MEDROXYPROGESTERONE ACETATE ON THE **EFFICACY** OF

CYTOTOXIC DRUGS STUDIES WITH HUMAN BREAST **CANCER**
CELLS IN **CULTURE**.

AU SHAIKH N A; OWEN A M; GHILCHIK M W; BRAUNSBURG H
CS DEP. CHEM. PATHOL., ST. MARY'S HOSP. MED. SCH., LONDON W2 1PG, UK.
SO INT J CANCER 43 (3). 1989. 458-463. CODEN: IJCNAW ISSN: 0020-7136
LA English
AB Human breast **cancer** cells (MCF-7) showed increased responses to methotrexate and vincristine after a 48-hr pretreatment with medroxyprogesterone acetate. The effect of the hormone, which was detectable at concentrations of between 10 and 100nM, was independent of its growth-inhibitory action. These findings confirm a previous clinical study and have important implications with regard to the management of advanced breast **cancer**.

L47 ANSWER 19 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 88:463205 BIOSIS

DN BA86:104924

TI EVALUATION OF A SOLUBLE TETRAZOLIUM-FORMAZAN ASSAY FOR CELL GROWTH AND DRUG SENSITIVITY IN **CULTURE** USING HUMAN AND OTHER **TUMOR** CELL LINES.

AU SCUDIERO D A; SHOEMAKER R H; PAULL K D; MONKS A; TIERNEY S; NOFZIGER T H; CURRENS M J; SENIFF D; BOYD M R

CS BUILD. 539, NATL. CANCER INST.-FREDERICK CANCER RES. FACILITY, FREDERICK, MD. 21701.

SO CANCER RES 48 (17). 1988. 4827-4833. CODEN: CNREA8 ISSN: 0008-5472

LA English

AB We have previously described the application of an automated microculture tetrazolium assay (MTA) involving dimethyl sulfoxide solubilization of cellular-generated 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT)-formazan to the in vitro assessment of drug effects on cell growth (M. C. Alley et al., Proc. Am. Assoc. **Cancer** Res. 27:389, 1986; M. C. Alley et al., **Cancer** Res. 48:589-601, 1988). There are several inherent disadvantages of this assay, including the safety hazard of personnel exposure to large quantities of dimethyl sulfoxide, the deleterious effects of this solvent on laboratory equipment, and the inefficient metabolism of MTT by some human cell lines. Recognition of these limitations prompted development of possible alternative MTAs utilizing a different tetrazolium reagent, 2,3-bis(2-methoxy-4-nitro-5-sulfophenyl)-5-[(phenylamino)carbonyl]-2H-tetrazolium hydroxide (XTT), which is metabolically reduced in value cells to a water-soluble formazan product. This reagent allows direct absorbance readings, therefore eliminating a solubilization step and shortening the microculture growth assay procedure. Most human **tumor** cell lines examined metabolized XTT less efficiently than MTT; however, the addition of phenazine methosulfate (PMS) markedly enhanced cellular reduction of XTT. In the presence of PMS, the XTT reagent yielded usable absorbance values for growth and **drug** sensitivity **evaluations** with a variety of cell lines. Depending on the metabolic reductive capacity of a given cell line, the optimal conditions for a 4-h XTT incubation assay were 50 .mu.g of XTT and 0.15 to 0.4 .mu.g of PMS per well. Drug profiles obtained with representative human **tumor** cell lines for several standard compounds utilizing the XTT-PMS methodology were similar to the profiles obtained with MTT. Addition of PMS appeared to have little effect on the metabolism of MTT. The new XTT reagent thus provides for a simplified, in vitro cell growth assay with possible

applicability to a variety of in vitro cell growth assay with possible applicability to a variety of problems in cellular pharmacology and biology. However, the MTA using the XTT reagent still shares many of the limitations and potential pitfalls of MTT or other tetrazolium-based assays.

- L47 ANSWER 20 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
 AN 88:345312 BIOSIS
 DN BR35:40154
 TI ENHANCED RECOVERY FROM MELPHALAN TREATMENT OF TUMOR CELLS IN COLLAGEN CULTURES.
 AU MILLER B E; HEPPNER G H
 CS MICHIGAN CANCER FOUNDATION, DETROIT, MI 48201.
 SO 79TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, NEW ORLEANS, LOUISIANA, USA, MAY 25-28, 1988. PROC AM ASSOC CANCER RES ANNU MEET 29 (0). 1988. 488. CODEN: PAMREA
 DT Conference
 LA English
- L47 ANSWER 21 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
 AN 88:345309 BIOSIS
 DN BR35:40151
 TI IN-VITRO CHEMOSENSITIVITY OF FRESH LUNG TUMORS IN THE ADHESIVE TUMOR-CELL CULTURE SYSTEM ATCCS VS. LUNG TUMOR CELL LINES IN THE TETRAZOLIUM ASSAY MTT IMPLICATIONS FOR DRUG SCREENING.
 AU TUENI E; SPITZER G; AJANI J A; BAKER F; FAN D
 CS M.D. ANDERSON HOSP. AND TUMOR INST., HOUSTON, TX 77030.
 SO 79TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, NEW ORLEANS, LOUISIANA, USA, MAY 25-28, 1988. PROC AM ASSOC CANCER RES ANNU MEET 29 (0). 1988. 487. CODEN: PAMREA
 DT Conference
 LA English
- L47 ANSWER 22 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
 AN 88:157656 BIOSIS
 DN BA85:81309
 TI COMPARISON OF TWO METHODS TO EVALUATE DRUG CYTOTOXICITY ON TUMOR CELL LINES CULTURED IN-VITRO.
 AU PINELLI A; TRIVULZIO S; VON HOFF D D; WARFEL L
 CS DEP. PHARMACOL., UNIV. MILAN, VIA VANVITELLI 32, MILAN.
 SO PHARMACOL RES COMMUN 19 (12). 1987. 913-923. CODEN: PLRCAT ISSN: 0031-6989
 LA English
- AB Some porphyrin compounds: P-NO₂ and CVRIV were screened for cytotoxic activity against HT-29, LOVO, human tumor cell lines. The new radiometric assay was used for all cell lines. The soft agar cloning system was also utilized. The tested compounds decrease the growth index, measured in the radiometric assay, as ¹⁴CO₂ production, and similarly depress the growth of tumor colonies on soft agar in the clonogenic assay. The cytotoxic effects of the compounds tested by these different methods were analysed statistically and resulted quantitatively similar. Based on these findings the radiometric assay represents a method, simple and rapid, which can be used as the clonogenic assay to screen new anticancer drugs.

L47 ANSWER 23 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 88:6733 BIOSIS

DN BA85:6733

TI COMPARISON OF ANTITUMOR ACTIVITY OF STANDARD AND INVESTIGATIONAL
DRUGS AT EQUIVALENT GRANULOCYTE-MACROPHAGE COLONY-FORMING
CELL INHIBITORY CONCENTRATIONS IN THE ADHESIVE TUMOR CELL
CULTURE SYSTEM AN IN-VITRO METHOD OF SCREENING NEW
DRUGS.

AU FAN D; AJANI J A; BAKER F L; TOMASOVIC B; BROCKS W A; SPTIZER G
CS M.D. ANDERSON HOSP. AND TUMOR INST., 1515 HOLCOMBE BLVD., BOX 47,
HOUSTON, TEX. 77030, USA.

SO EUR J CANCER CLIN ONCOL 23 (10). 1987. 1469-1476. CODEN: EJCODS
ISSN: 0277-5379

LA English

AB We compared the in vitro growth inhibition of primary human
tumor cells in the adhesive tumor cell culture
system (ATCCS), exposed to the investigational agents caracemide,
spirogermanium and taxol and to standard chemotherapy agents at
equitoxic concentrations for granulocyte-macrophage colony-forming
cells (GM-CFC) in vitro. Clinically active standard agents tested at
up to GM-CFC 90% inhibitory concentrations (IC90) resulted in in
vitro activity (.gtoreq. 50% tumor growth inhibition) in at
least 30% of tumors tested. In vitro responses for taxol,
caracemide and spirogermanium were 78%, 9% and 7%, respectively. This
paper proposes a model that incorporates two hypotheses: (1)
myelotoxic drugs which inhibit tumor growth at
concentrations equal to or less than equitoxic GM-CFC ICs will
demonstrate clinical activity; and (2) both myelotoxic and particular
nonmyelotoxic drugs inactive in vitro at these doses will not be
active clinically. If this drug screening concept
is valid, taxol may be clinically more active than caracemide and
spirogermanium.

L47 ANSWER 24 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 87:486466 BIOSIS

DN BA84:121109

TI CHEMOSENSITIVITY PROFILES OF PRIMARY AND CULTURED
HUMAN RETINOBLASTOMA CELLS IN A HUMAN TUMOR CLONOGENIC
ASSAY.

AU INOMATA M; KANEKO A

CS PHARM. DIV., NAT. CANCER CENT. RES. INST., NATL. CANCER CENT. HOSP.,
TSUKIJI 5-1-1, CHUO-KU, TOKYO 104.

SO JPN J CANCER RES (GANN) 78 (8). 1987. 858-868. CODEN: JJCREP ISSN:
0910-5050

LA English

AB The drug sensitivity of retinoblastoma cells obtained from 14 fresh
primary materials (13 from enucleation and 1 from autopsy) and 2
cultured lines (Y-79 and WERI-Rb1) was determined using the human
tumor clonogenic assay developed by Hamburger and Salmon.
Components of the conventional soft agar medium were slightly
modified to make them suitable for growing primary retinoblastoma
cells. More than 5 colonies were formed by all 14 primary samples
tested from the 500 .times. 103 cells plated. More than 30 colonies
per dish were formed from the 13 samples, with a median plating
efficiency of 0.033% (0.005-0.400), and these were used in the in
vitro measurements of drug chemosensitivities. They showed

homogeneous sensitivity to the representative alkylating agent L-phenylalanine mustard; 13 out of 14 showed a decrease in the colony formation of more than 70%. The other drugs which were effective (more than 70% colony inhibition) against the primary retinoblastoma cells were: doxorubicin (7 out of 13), mitomycin C (7 out of 13), actinomycin D (4 out of 13), cis-diamminedichloroplatinum(II) (3 out of 13), nimustine (1 out of 13), and peplomycin (1 out of 13). Vincristine, bleomycin, 5-fluorouracil, methotrexate, dacarbazine, and cytosine arabinoside were not effective. When the chemosensitivity of retinoblastoma cells of the two established cell lines was examined by the same method, only L-phenylalanine mustard was effective against Y-79, and no drug was effective against WERI-Rb1.

L47 ANSWER 25 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 87:388228 BIOSIS

DN BR33:68368

TI HUMAN CELL CULTURES FOR SCREENING ANTI-CANCER DRUGS.

AU BERTONCELLO I; BRADLEY T R

CS CELL BIOL. GROUP, PETER MACCALLUM RES. LAB., PETER MACCALLUM CANCER INST., 481 LITTLE LONSDALE ST., MELBOURNE, VICTORIA 3000, AUST.

SO TRENDS PHARMACOL SCI 8 (7). 1987. 249-251. CODEN: TPHSDY ISSN: 0165-6147

LA English

L47 ANSWER 26 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 87:212163 BIOSIS

DN BA83:109793

TI INTER-EXPERIMENT VARIATION AND DEPENDENCE ON CULTURE CONDITIONS IN ASSAYING THE CHEMOSENSITIVITY OF HUMAN SMALL CELL LUNG CANCER CELL LINES.

AU ROED H; CHRISTENSEN I J; VINDELOV L L; SPANG-THOMSEN M; HANSEN H H

CS DEP. ONCOL. II, FINSEN INST., 49 STRANDBOULEVARDEN, DK-2100 COPENHAGEN, DEN.

SO EUR J CANCER CLIN ONCOL 23 (2). 1987. 177-186. CODEN: EJCODS ISSN: 0277-5379

LA English

AB Sensitivity of five human small cell lung cancer cell lines to doxorubicin was assessed by a double layer agar technique using two different bottom-layers. Neither of the bottom-layers provided proportionality between numbers of cells plated and number of colonies, but they were correlated by a logarithmic function. Even after correction for lack of proportionality the two assay system provided significantly different dose-response curves. The stability of the chemosensitivity was tested after 25-30 weeks continuous in vitro culture or prolonged storage in liquid nitrogen. One cell line underwent significant changes after continuous in vitro culture whereas the cell lines tested after prolonged storage in liquid nitrogen showed only minor changes. It is concluded that instead of considering the concentration necessary to achieve a certain degree of cell kill (e.g. ID50) in one experiment on one cell line, dose-response curves obtained on several cell lines in different assay systems should be used in the evaluation of new drugs.

L47 ANSWER 27 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS

AN 87:107442 BIOSIS
 DN BA83:56420
 TI OBSERVATION ON COLONY FORMATION OF HUMAN TUMOR STEM CELLS
 BY USING MODIFIED IN-VITRO TWO LAYER AGAR CULTURE SYSTEM.
 AU CHAO W; PEN X-E; YE Y
 CS RES. LAB. PHARMACOLOGY, HUNAN MED. COLL.
 SO BULL HUNAN MED COLL 11 (3). 1986. 285-288. CODEN: HYHPDO ISSN:
 0253-3170
 LA Chinese
 AB The influence of homoharringtonine (H), rubescensine-a(Rub-A) and
 some other standard antineoplastic drugs, including ADM, VCR and DDP,
 on clonogenic formation of seven types of human solid tumors
 was observed by using a little modified Hamburger-Salmon's in vitro
 two layer agar culture system (2-LACS). The results revealed that 5
 out of 16 human tumor samples were sensitive to HH; 5 out
 of 7 to Rub-A. In addition, obvious selective anticancer activities
 were observed with three standard anticancer drugs in the system. The
 number of sensitive samples were 10/16, 4/13 and 4/8 for ADM, VCR and
 DDP, respectively. It is suggested that the method modified by our
 laboratory could be used in determination of sensitivity of human
 tumor stem cells to anticancer drugs.

L47 ANSWER 28 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
 AN 86:144237 BIOSIS
 DN BA81:54653
 TI A COMPARISON OF TWO CULTURE TECHNIQUES AN IN-VITRO AND AN
 IN-VIVO TUMOR COLONY-FORMING ASSAY.
 AU SLEE P H T J; WILLEMZE R; VAN OOSTEROM A T; LURVINK E; VAN DEN BERG L
 CS DIV. CLINICAL ONCOL., DEP. MED., LEIDEN UNIV. MED. CENT., LEIDEN,
 NETHERLANDS.
 SO BR J CANCER 52 (5). 1985. 713-718. CODEN: BJCAAI ISSN: 0007-0920
 LA English
 AB Twenty-one identical tumour specimens were cultured both in
 the Plasma-Clot Diffusion Chamber (PCDC) Technique and the Human
 Tumour Colony-forming Assay (HTCA). The culture results
 achieved in the PCDC-technique were clearly superior to the HTCA: in
 the PCDC the mean and median plating efficiency (PE) was 0.156 and
 0.147, in the HTCA 0.103 and 0.028%; adequate growth rate in the
 PCDC-technique was 67% and in the HTCA 38%. Fewer cells were required
 for plating in the PCDC-technique: 6.4 .times. 104 vs. 2.6 .times.
 105 in the HTCA. The mean and median coefficient of variation of the
 colony numbers in the PCDC-technique appeared much higher: 27.3 and
 37.3 vs. 11.2 and 11.1% in the HTCA. The relation between the PEs
 obtained for the same specimen in the two techniques was compared. No
 positive correlation was found, which can possibly be ascribed to
 technical shortcomings in both techniques.

L47 ANSWER 29 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
 AN 86:144235 BIOSIS
 DN BA81:54651
 TI TIME COURSE OF OVARIAN TUMOR GROWTH IN SOFT AGAR
 CULTURE.
 AU VERHEIJEN R H M; FEITZ W F J; KENEMANS P; VOOYS G P; HERMAN C J
 CS INST. PATHOL., ST. RADBOUD UNIV. HOSP., NIJMEGEN, NETHERLANDS.
 SO BR J CANCER 52 (5). 1985. 707-712. CODEN: BJCAAI ISSN: 0007-0920
 LA English
 AB Single time point assessment is usually employed in the Human

Tumour Cloning System as the only parameter for in vitro growth. This does not seem to give a fair expression of the dynamic biological properties of **tumour** growth and time dependent effects, e.g. of cytotoxic drugs. We studied the time course of colony formation in temporal growth patterns (TGP) and compared this method of growth evaluation with conventional single time point assessment in 57 samples of ovarian **tumour** cultures in the HTCS. A first advantage of the use of TGP is that more cultures become evaluable, as this assessment over time can detect a rise in the number of colonies in dishes where colony-like clumps have initially been seeded. Thus only 28 of the cultures were evaluable for single time point assessment, whereas 57 were available for TGP evaluation. Growth was more often seen at TGP evaluation (14/57) than at single day assessment (8/57). Evaluation of growth over the course of time potentially allows detection of sensitivity to drugs. Furthermore TGP reflect the dynamics of biological growth. These features cannot be studied in single time point assessment.

L47 ANSWER 30 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 86:23341 BIOSIS
DN BR30:23341
TI ORGAN CULTURE.
AU MULEA R
CS INSTITUTUL ONCOLOGIC CLUJ-NAPOCA.
SO REV CHIR ONCOL RADIOL O R L OFTALMOL STOMATOL SER ONCOL 24 (2). 1985.
133-139. CODEN: ONCODU
LA Romanian

L47 ANSWER 31 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 85:390431 BIOSIS
DN BA80:60423
TI CULTURED HUMAN HEPATOMA CELL BEL-7404 FOR ANTICANCER
DRUGS SCREENING.
AU YANG J-L; SHEN Z-M; SUN Y-F; HAN J-X; XU B
CS SHANGHAI INST. MATERIAL MEDICA, CHIN. ACAD. SCIENCES, SHANGHAI
200031.
SO ACTA PHARMACOL SIN 6 (2). 1985. 144-148. CODEN: CYLPDN ISSN:
0253-9756
LA Chinese
AB A quantitative method of **tumor** cell culture for evaluating anticancer agents in vitro was established. Typical cell-growth curve was seen when human hepatoma (BEL-7404) 2.5 .times. 10² - 2.5 .times. 10⁴ cells/well were placed in plastic microtiter plates. The amount of radioactivity of [3H]leucine incorporated into cells was used to assay the cell-growth rate. 10-Hydroxycamptothecin (1-100 .mu.g/ml) significantly inhibited the growth of BEL-7404. The incorporation of [3H]leucine into the protein of **tumor** cells was inhibited by 31-71%. Among 40 drugs tested, harringtonine, homoharringtonine and nevadensin markedly inhibited the growth of BEL-7404 cells.

L47 ANSWER 32 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 84:276317 BIOSIS
DN BA78:12797
TI CELLULAR PHARMACO KINETICS OF DOXORUBICIN IN CULTURED MOUSE SARCOMA CELLS ORIGINATING FROM AUTOCHTHONOUS TUMORS.
AU NGUYEN-NGOC T; VRIGNAUD P; ROBERT J
CS FOND. BERGONIE, 180, RUE DE SAINT-GENES, F-330076 BORDEAUX CEDEX, FR.

- SO ONCOLOGY (BASEL) 41 (1). 1984. 55-60. CODEN: ONCOBS ISSN: 0030-2414
 LA English
- AB The cellular pharmacology of doxorubicin [and daunorubicin] in a line of mouse sarcoma cells isolated from a dimethylbenzanthracene-induced autochthonous **tumor** was examined. The cytotoxicity of the drugs was studied as a function of the exposure dose and of the exposure time to the **drug**. Cytotoxicity was **evaluated** as the inhibition of the incorporation of [3H-methyl]-thymidine in the cellular nucleic acids. Intracellular drug concentrations were measured by spectrofluorometry. The intracellular drug concentration was a linear function of the extracellular drug concentration up to 5 .mu.g/ml; the cytotoxicity was an exponential function of the exposure dose up to 1 .mu.g/ml, but it was not an exponential function of the exposure time: the cytotoxicity may therefore be very different for similar total drug exposures. Incubation with a low dose for a long time did not provide a cytotoxicity as high as that obtained with a high dose for a short period of time. The role of the peak concentration of doxorubicin for its maximal action in the target cell is emphasized.
- L47 ANSWER 33 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
 AN 83:216226 BIOSIS
 DN BA75:66226
 TI DIRECT CLONING OF HUMAN BREAST **CANCER** IN SOFT AGAR **CULTURE**.
- AU SANDBACH J; VON HOFF D D; CLARK G; CRUZ A B JR; OBRIEN M; S CENTRAL TEX HUM TUMOR CLONING GROUP
 CS AUSTIN DIAGNOSTIC CLINIC, AUSTIN, TEX.
 SO CANCER (PHILA) 50 (7). 1982. 1315-1321. CODEN: CANCAR ISSN: 0008-543X
 LA English
- AB A human **tumor** cloning system was utilized to grow human breast carcinoma. A total of 225 specimens were placed in culture; 132 were from primary chest **cancer** specimens and 93 were from metastatic lesions. Of these, 71% of the primary breast carcinomas and 75% of metastases formed .gtoreq. 5 colonies per 500,000 cells plated. Forty-five percent of the primary breast carcinomas and 52% of the metastases formed enough colonies (.gtoreq. 30 colonies per 500,000 cells plated) to perform meaningful in vitro drug testing. Estrogen receptor status did not influence the percentage of **tumors** which formed colonies in vitro. Histologic and nude mouse studies provided confirmatory evidence that the colonies were composed of breast **cancer** cells. In 176 in vitro chemotherapeutic drug tests, the anticancer agents commonly used clinically for treatment of breast **cancer**, i.e., Adriamycin, 5-fluorouracil, etc., showed some in vitro activity. This activity was not as dramatic as is seen in the clinic with these conventional agents. Future work should concentrate on improving the number of colonies which form from breast **cancer** specimens and on prospective use of the system for screening for new agents in the treatment of human breast **cancer**.
- L47 ANSWER 34 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
 AN 83:169928 BIOSIS
 DN BA75:19928
 TI RAPID **ASSAY** FOR EVALUATING THE **CHEMO** **SENSITIVITY** OF HUMAN **TUMORS** IN SOFT AGAR

CULTURE.

AU TANIGAWA N; KERN D H; HIKASA Y; MORTON D L
 CS DEP. SURGERY, UNIV. KYOTO, SAKYO-KU, KYOTO, JAPAN.
 SO CANCER RES 42 (8). 1982. 2159-2164. CODEN: CNREA8 ISSN: 0008-5472
 LA English
 AB Assays that measure [3H]thymidine incorporation by cells plated in soft agar were investigated to identify a rapid method for assessing chemosensitivity of **tumor** cells. [The drugs for in vitro study included bleomycin, carmustine, cis-platinum, dacarbazine, dihydroxyanthracenedione, doxorubicin, 5-fluorouracil, acrydinyl anisidide, melphalan, methotrexate, mitomycin C, phenylalanine disodium, vinblastine, vincritine, and interferon.] Six established cell lines (5 melanomas and 1 colon carcinoma) and cells prepared from 23 primary or metastatic **tumors** (10 melanomas, 5 colon adenocarcinomas, 3 lung carcinomas, 2 ovarian adenocarcinomas, 1 breast adenocarcinoma, and 1 leiomyosarcoma) were tested. The end point of 3H incorporation was measured by autoradiographs (labeling index) and scintillation counting (cpm) after 24-h labeling. When results were compared, there was a strong correlation between the 2 assays ($P < 0.0001$). However, the scintillation counting assay had major advantages: counting incorporated radioisotope was technically easier than the autoradiographic method; the DNA synthesis rate of the whole **tumor** cell population could be evaluated, not that of **tumor** colony-forming cells alone; and the sampling error was minimized since the procedure was done automatically. There was significant association between cpm values 48-72 h after plating and the number of colonies formed at 2-4 wk in control dishes ($P < 0.001$). Eighteen of 23 surgical specimens (78%) and all 4 cell lines were evaluable. Chemosensitivity was assessed after 48 h of plating with alkylating agents, antibiotics, and Vinca alkaloids and after 72 h with 5-fluorouracil and methotrexate. Results of 93 courses of drug-related inhibition of colony formation were compared to results of the scintillation assay. An 80% or greater reduction of [3H]thymidine incorporation was correlated with a 75% or greater decrease in colony growth ($P < 0.0001$). Thus, this scintillation assay accurately predicted drug-**tumor** interactions with 5 days that resulted in a 75% or greater decrease in colonies.

L47 ANSWER 35 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
 AN 82:32806 BIOSIS
 DN BR22:32806
 TI THE SOFT AGAR **CULTURE** METHOD FOR MALIGNANT **TUMORS**
 1ST RESULTS WITH NEURO BLASTOMA LINES AND NATIVE **TUMORS**.
 AU DANNECKER G; TREUNER J; BUCK J; NIETHAMMER D
 CS DIV. PEDIATRIC HEMATOL., UNIV. TUEBINGEN, TUEBINGEN, GERMANY.
 SO MEETING OF THE EUROPEAN SOCIETY FOR PAEDIATRIC RESEARCH, EUROPEAN SOCIETY FOR PAEDIATRIC GASTROENTEROLOGY AND NUTRITION, EUROPEAN SOCIETY FOR PAEDIATRIC HAEMATOLOGY AND IMMUNOLOGY, EUROPEAN PAEDIATRIC RESPIRATORY SOCIETY AND THE WORKING GROUP FOR MINERAL METABOLISM, BERNE, SWITZERLAND, SEPT. 23-26, 1981. PEDIATR RES 15 (8). 1981. 1207. CODEN: PEREBL ISSN: 0031-3998
 DT Conference
 LA English

L47 ANSWER 36 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
 AN 81:7099 BIOSIS
 DN BR20:7099

TI LABELING INDEX DEPRESSION IN HUMAN TUMOR CELLS
CULTURED IN DOUBLE LAYER AGAR A POTENTIAL CHEMO
SENSITIVITY ASSAY.

AU ELSON D L; LIVINGSTON R B; COLTMAN C A JR; VON HOFF D D
CS UNIV. TEX. HEALTH SCI. CENT., SAN ANTONIO, TEX. 78284, USA.
SO 71ST ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH,
SAN DIEGO, CALIF., USA, MAY 28-31, 1980. PROC AM ASSOC CANCER RES AM
SOC CLIN ONCOL 21 (0). 1980. 164. CODEN: PAAOD8
DT Conference
LA English

L47 ANSWER 37 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 80:204610 BIOSIS

DN BA69:79606

TI PROPERTIES OF A CELL CULTURE LINE DERIVED FROM LYMPHO
SARCOMA P-1798.

AU THOMPSON E A JR

CS DEP. BIOL., UNIV. S.C., COLUMBIA, S.C. 29208, USA.

SO MOL CELL ENDOCR 17 (2). 1980. 95-102. CODEN: MCEND6 ISSN: 0303-7207

LA English

AB In many mammalian species cells of lymphatic origin have the unusual property of cytolysis in the presence of pharmacological concentrations of adrenal glucocorticoids. Although the underlying mechanism is not well understood, the phenomenon was clinically exploited to the extent that natural and synthetic glucocorticoids were extensively used in the treatment of lymphoproliferative diseases. The efficacy of such chemotherapy is diminished by the fact that remission is often followed by appearance of cells which are resistant to the cytolytic effects of the hormone. A cell culture line was derived from mouse lymphosarcoma P1798. Cultures of this line grow exponentially with a doubling time of about 20-24 h. Cells will not divide in the presence of 10^{-8} M dexamethasone [D]. Half-maximal inhibition of proliferation occurs at about 10^{-9} M. Half-maximal inhibition of [3H] thymidine incorporation occurs at somewhat higher concentrations. When cells are cultured in the presence of 2×10^{-7} M D they remain 88% viable after 5 days. No decrease in cell number occurs. These cells can be rescued by in vivo passage and they respond in culture to D in exactly the same fashion as do untreated cells. Both D rescued and untreated cultured cells contain about 104 D receptor sites which bind with a K_d of 4×10^{-9} M. Cultured cells retain the ability to proliferate both subcutaneously and in ascites. The properties of such tumors resemble those of the parental tumor cell line.

L47 ANSWER 38 OF 41 BIOSIS COPYRIGHT 1998 BIOSIS
AN 77:145460 BIOSIS

DN BA63:40324

TI SYNTHESIS AND BIOLOGICAL ACTIVITY OF 3 5 DI NITRO-4 1H-PURIN-6-YL
THIO BENZOATES AND 3 5 DI NITRO-2 1H-PURIN-6-YL THIO BENZOATES PRO
DRUGS OF 6 MERCAPTO PURINE.

AU DRAWBAUGH R; BOUFFARD C; STRAUSS M

SO J MED CHEM 19 (11). 1976 1342-1345. CODEN: JMCMAR ISSN: 0022-2623

LA Unavailable

AB A series of prodrug modifications of 6-mercaptopurine (6-MP) containing dinitrobenzoate ester moieties with varying chain length was prepared. These compounds were cytotoxic in several cell culture

Gitomer 09/039,957

=> fil medline

FILE 'MEDLINE' ENTERED AT 13:54:13 ON 03 DEC 1998

FILE LAST UPDATED: 29 OCT 1998 (19981029/UP). FILE COVERS 1966 TO DATE.

MEDLINE UPDATES ON HOLD UNTIL AFTER THE ANNUAL RELOAD HAS BEEN COMPLETED. NOTICE WILL BE GIVEN ONCE THE RELOAD IS COMPLETED AND RELOAD DETAILS WILL BE FOUND IN HELP RLOAD.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

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(FILE 'HOME' ENTERED AT 13:41:00 ON 03 DEC 1998)

FILE 'MEDLINE' ENTERED AT 13:41:46 ON 03 DEC 1998

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      E TUMOR CELLS, CULTURED/CT
      E E3+ALL
L1      104252 S TUMOR CELLS, CULTURED+NT/CT
      E DRUG SCREENING ASSAYS, ANTITUMOR/CT
      E E3+ALL
L2      6535 S DRUG SCREENING ASSAYS, ANTITUMOR+NT/CT
L3      3416 S L1 AND L2
L4      12296 S L1 (L) DE./CT
L5      1289 S L4 AND L3
L6      41 S MONOLAYER# AND L5
L7      4004 S DRUG SCREENING ASSAYS, ANTITUMOR/CT
L8      937 S L7 AND L5
L9      26 S L8 AND MONOLAYER#
L10     0 S ANTINEOPLASTIC AGENTS+NT/FT
L11     419987 S ANTINEOPLASTIC AGENTS+NT/CT
L12     836 S L11 AND L8
L13     2475 S MULTICELLULAR
L14     11 S L12 AND L13
L15     11 S L8 AND L13
L16     0 S L12 AND MONOLAYERA#
L17     19 S L12 AND MONOLAYER#
L18     156 S TERASAKI
L19     2 S L18 AND L2
L20     25 S L15 OR L17 OR L19
L21     3 S L7 (L) IS
L22     27 S L20 OR L21
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FILE 'MEDLINE' ENTERED AT 13:54:13 ON 03 DEC 1998

=> d .med 122 1-27

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L22 ANSWER 1 OF 27 MEDLINE
AN  1998387318 MEDLINE
DN  98387318
TI  Tolyporphin: a natural product from cyanobacteria with potent
    photosensitizing activity against tumor cells in vitro and in vivo.
AU  Morli`ere P; Mazi`ere J C; Santus R; Smith C D; Prinsep M R; Stobbe
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C C; Fenning M C; Golberg J L; Chapman J D
 CS Laboratoire de Photobiologie (Institut National de la Sante et de la Recherche Medicale U 312), Museum National d'Histoire Naturelle, Paris, France.
 SO CANCER RESEARCH, (1998 Aug 15) 58 (16) 3571-8.
 Journal code: CNF. ISSN: 0008-5472.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; Cancer Journals
 EM 199811
 EW 19981103
 AB Tolyporphin (TP), a porphyrin extracted from cyanobacteria, was found to be a very potent photosensitizer of EMT-6 tumor cells grown both in vitro as suspensions or **monolayers** and in vivo in tumors implanted on the backs of C.B17/Icr severe combined immunodeficient mice. Thus, during photodynamic treatment (PDT) of EMT-6 tumor cells in vitro, the photokilling effectiveness of TP measured as the product of the reciprocal of D50 (the light dose necessary to kill 50% of cells) and the concentration of TP is approximately 5000 times higher than that of Photofrin II (PII), the only PDT photosensitizer thus far approved for clinical trials. TP almost exclusively localizes in the perinuclear region and specifically in the endoplasmic reticulum (ER), as shown by microspectrofluorometry on single living EMT-6 cells costained with the ER and/or Golgi fluorescent vital probes, 3,3'-dihexyloxacarbocyanine iodide and N-[4,4-difluoro-(5,7-dimethyl-BODIPY)-1-pentanoyl]-D-erythro-sphingosine (Molecular Probes, Eugene, OR). As a result, the singlet oxygen-mediated photodynamic activity of TP induces an effective inactivation of the acyl CoA:cholesterol-O-acyltransferase, a sensitive marker of ER membrane integrity and alterations of the nuclear membrane. In vivo, with the EMT-6 mouse tumor model, an exceptional effectiveness is also observed as compared to that of PII and other second generation photosensitizers of the pheophorbide class, which are themselves much more potent than PII. The outstanding PDT activity of TP observed in vivo may be due to its unique biodistribution properties, in particular much less extraction by the liver, resulting in a higher delivery to other tissues, including tumor.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Antineoplastic Agents: PK, pharmacokinetics
***Antineoplastic Agents: TU, therapeutic use**
 Coenzyme A-Transferases: DE, drug effects
 Coenzyme A-Transferases: ME, metabolism
 Cyanobacteria
Dihematoporphyrin Ether: TU, therapeutic use
Drug Screening Assays, Antitumor
 Mammary Neoplasms, Experimental: DT, drug therapy
 Mammary Neoplasms, Experimental: ME, metabolism
 Mice
 Mice, SCID
 *Photochemotherapy
 Photosensitizing Agents: PK, pharmacokinetics
 *Photosensitizing Agents: TU, therapeutic use
 Porphyrins: PK, pharmacokinetics
 *Porphyrins: TU, therapeutic use
Tumor Cells, Cultured: DE, drug effects

L22 ANSWER 2 OF 27 MEDLINE
 AN 97306569 MEDLINE
 DN 97306569
 TI Indomethacin enhances the cytotoxicity of VCR and ADR in human pulmonary adenocarcinoma cells.
 AU Kobayashi S; Okada S; Yoshida H; Fujimura S
 CS Department of Thoracic Surgery, Tohoku University, Sendai.
 SO TOHOKU JOURNAL OF EXPERIMENTAL MEDICINE, (1997 Mar) 181 (3) 361-70.
 Journal code: VTF. ISSN: 0040-8727.
 CY Japan
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199709
 EW 19970904
 AB The ability of anti-inflammatory agents to modulate cellular sensitivity to anticancer drugs was investigated for pulmonary carcinoma cells in vitro. We examined the drug sensitivity of two pulmonary adenocarcinoma cell lines (76-2, 77-4) in the presence of two drugs, an anticancer drug and an anti-inflammatory agent, for 72 hr by the 3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay with 96 well plates. Anticancer drugs used for screening test were cyclophosphamide (CPM), mitomycin C (MMC), adriamycin (ADR), 5-fluorouracil (5FU), vindesine (VDS), cisplatin (CDDP), cytarabine (Ara C), methotrexate (MTX), etoposide (VP-16), and vincristine (VCR). Anti-inflammatory agents examined as modulators to anticancer drugs were aspirin, mefenamic acid, ibuprofen, sulindac, piroxicam, phenacetin, diclofenac, ketoprofen, tolmetin and indomethacin. Screening tests showed indomethacin to be the most effective modulator, resulting in more than a 3-fold increase in cytotoxicity of VCR as compared with that produced by VCR alone. Study of each of the ten anticancer drugs in combination with indomethacin showed VCR to be the most effective anticancer drug in this combination. In 76-2 cells, the concentration of VCR producing 50% growth inhibition (IC50) for VCR alone and VCR in combination with 2 micrograms/ml indomethacin were 1.58 +/- 0.16 and 0.52 +/- 0.1 ng/ml respectively, which represents a 3-fold decrease. In 77-4 cells, the IC50 for VCR alone and VCR in combination with 2 micrograms/ml indomethacin were 2.86 +/- 0.2 and 0.52 +/- 0.11 ng/ml respectively, which represents a 3.8-fold decrease. Our studies indicate that clinically achievable concentrations of indomethacin may be useful in modulating VCR resistance in human pulmonary adenocarcinoma cells, so that combined use of VCR and indomethacin may be of potential clinical significance in the treatment of lung cancer.
 CT Check Tags: Human
 *Adenocarcinoma: DT, drug therapy
 *Adjuvants, Pharmaceutic: PD, pharmacology
 Doxorubicin: PD, pharmacology
 *Doxorubicin: TO, toxicity
 Drug Combinations
 Drug Screening Assays, Antitumor: IS, instrumentation
 Drug Screening Assays, Antitumor: MT, methods
 Dyes
 Etoposide: PD, pharmacology
 *Indomethacin: PD, pharmacology

*Lung Neoplasms: DT, drug therapy
 Tetrazolium Salts: DU, diagnostic use
 Thiazoles: DU, diagnostic use
 Tumor Cells, Cultured
 Vincristine: PD, pharmacology
 *Vincristine: TO, toxicity

L22 ANSWER 3 OF 27 MEDLINE

AN 97070509 MEDLINE

DN 97070509

TI Association of docetaxel/paclitaxel with irradiation in ovarian carcinoma cell lines in bidimensional (sulforhodamine B assay) and tridimensional (spheroids) cultures.

AU Griffon-Etienne G; Merlin J L; Marchal C

CS Laboratoire de Recherche en Oncologie, Centre Alexis Vautrin, Vandoeuvre-les-Nancy Cedex, France.

SO ANTI-CANCER DRUGS, (1996 Aug) 7 (6) 660-70.

Journal code: A9F. ISSN: 0959-4973.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199705

EW 19970503

AB The association of taxoid derivatives (paclitaxel and docetaxel) with irradiation was evaluated in ovarian carcinoma cell lines (A2780 and CAVEOC-2) using the **multicellular** tumor spheroids (MTS) tridimensional model and compared to the conventional bidimensional model. The radiosensitivity parameters were the surviving fraction at 2 Gy, and alpha calculated using the linear-quadratic model for **monolayer** culture, the residual/control volume ratios at 2 Gy (RSV2) and doses inducing 50% decrease in MTS number (SCD50) calculated for spheroids. In A2780 **monolayer** culture, the combination was synergistic for paclitaxel and additive for docetaxel. In spheroids, both compounds induced a decrease in RSV2 and SCD50 in the two cell lines, and their combination with radiation was additive. Therefore, the radiosensitizing effect of taxoid derivatives was not constant in ovarian cell lines. The different results achieved in **monolayer** culture and in spheroids may suggest higher drug incorporation and fixation through the multiple cell layers of the spheroids than in **monolayers**.

CT Check Tags: Comparative Study; Female; Human; Support, Non-U.S. Gov't

*Adenocarcinoma: TH, therapy

*Antineoplastic Agents, Phytogenic: PD, pharmacology

Combined Modality Therapy

Dose-Response Relationship, Drug

Dose-Response Relationship, Radiation

*Drug Screening Assays, Antitumor: MT, methods

*Ovarian Neoplasms: TH, therapy

*Paclitaxel: AA, analogs & derivatives

*Paclitaxel: PD, pharmacology

Tumor Cells, Cultured: DE, drug effects

Tumor Cells, Cultured: RE, radiation effects

L22 ANSWER 4 OF 27 MEDLINE

AN 97020276 MEDLINE
 DN 97020276
 TI Establishment and characterization of four human medulloblastoma-derived cell lines.
 AU Keles G E; Berger M S; Srinivasan J; Kolstoe D D; Bobola M S; Silber J R
 CS Department of Neurological Surgery University of Washington, Seattle 98195-6470, USA.
 NC K08 NS01253 (NINDS)
 T32 NS07144 (NINDS)
 SO ONCOLOGY RESEARCH, (1995) 7 (10-11) 493-503.
 Journal code: BBN. ISSN: 0965-0407.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199704
 EW 19970404
 AB We have established four cell lines, UW228-1, UW228-2, UW228-3 and UW443, from two posterior fossa medulloblastomas. The three UW228 sublines originated from a tumor with a diploid DNA content, while the tumor of origin of UW443 was predominantly tetraploid. Both tumors displayed areas of immunopositivity for synaptophysin and glial fibrillary acidic protein. All four cell lines have been grown as **monolayers** in continuous culture for 50 to 200 passages, are not contact inhibited at high density, and form colonies in soft agar. The UW228 sublines are aneuploid, have similar modal chromosome numbers, similar chromosomal duplications and identical marker chromosomes, and display loss of heterozygosity for identical sequences at the distal end of chromosome 17p. UW443 is diploid and also shows loss of heterozygosity for a distal sequence on chromosome 17p. All lines are immunopositive for two or more neurofilament proteins, three lines (UW228-1, UW228-2 and UW443) are immunopositive for synaptophysin, and none are immunopositive for glial fibrillary acidic protein. The lines differ in sensitivity to the alkylating agents 1,3-bis(2-chloroethyl)-1-nitrosourea and N-methyl-N'-nitro-N-nitrosoguanidine. They also differ in dependence on the DNA repair protein O6-methylguanine-DNA methyltransferase for alkylating agent resistance and in levels of the DNA repair activities apurinic/apyrimidinic endonuclease and DNA polymerase beta. These properties establish UW228-1, UW228-2, UW228-3 and UW443 as four new, phenotypically distinct medulloblastoma-derived cell lines.
 CT Check Tags: Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antineoplastic Agents, Alkylating: PD, pharmacology
 Cell Division: DE, drug effects
 Cell Division: PH, physiology
 Cerebellar Neoplasms: DT, drug therapy
 Cerebellar Neoplasms: GE, genetics
 *Cerebellar Neoplasms: PA, pathology
 Child
Drug Screening Assays, Antitumor
 Immunohistochemistry
 Karyotyping
 Medulloblastoma: DT, drug therapy
 Medulloblastoma: GE, genetics

*Medulloblastoma: PA, pathology
 *Tumor Cells, Cultured: DE, drug effects
 *Tumor Cells, Cultured: PA, pathology

L22 ANSWER 5 OF 27 MEDLINE
 AN 96302453 MEDLINE
 DN 96302453
 TI Daunorubicin and doxorubicin but not BCNU have deleterious effects on organotypic **multicellular** spheroids of gliomas.
 AU Kaaijk P; Troost D; de Boer O J; Van Amstel P; Bakker P J; Leenstra S; Bosch D A
 CS Department of Neurosurgery, University of Amsterdam, Graduate school Neurosciences Amsterdam, The Netherlands.
 SO BRITISH JOURNAL OF CANCER, (1996 Jul) 74 (2) 187-93.
 Journal code: AV4. ISSN: 0007-0920.
 CY SCOTLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; Cancer Journals
 EM 199610
 AB In the present study organotypic **multicellular** spheroids (OMS) were used to study the effects of chemotherapeutic agents on malignant gliomas. Compared with the frequently used cell line models, OMS have several advantages with respect to the preservation of the cellular heterogeneity and the structure of the original tumour. OMS prepared from seven glioma specimens were treated with 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU), daunorubicin or doxorubicin. After exposure to these drugs, the histology and cell proliferation of the OMS were analysed by immunohistochemistry and image analysis. Furthermore, the expression of P-glycoprotein (P-gp) and multidrug resistance-related protein (MRP), which both can contribute to resistance to daunorubicin and doxorubicin, were immunohistochemically investigated. We found that OMS from gliomas are sensitive for daunorubicin and doxorubicin but not for BCNU in terms of tissue destruction and decrease in cell proliferation. In addition, all gliomas were P-gp and MRP negative, which is in accordance with the sensitivity for daunorubicin and doxorubicin. Considering the potential use of several new alternative drug delivery methods, such as intratumoural implantation of drug-impregnated polymers or liposomal encapsulation of cytostatic drugs, daunorubicin and doxorubicin might be effective in the treatment of malignant gliomas.
 CT Check Tags: Comparative Study; Human
 *Antibiotics, Anthracycline: PD, pharmacology
 *Antineoplastic Agents, Alkylating: PD, pharmacology
 ABC Transporters: AN, analysis
 Brain Neoplasms: CH, chemistry
 *Brain Neoplasms: DT, drug therapy
 Brain Neoplasms: PA, pathology
 *Carmustine: PD, pharmacology
 Cell Division: DE, drug effects
 *Daunorubicin: PD, pharmacology
 *Doxorubicin: PD, pharmacology
 Drug Screening Assays, Antitumor
 Glioma: CH, chemistry
 *Glioma: DT, drug therapy
 Glioma: PA, pathology

Immunohistochemistry
P-Glycoprotein: AN, analysis
Spheroids: DE, drug effects
Tumor Cells, Cultured

L22 ANSWER 6 OF 27 MEDLINE

AN 96275788 MEDLINE

DN 96275788

TI Induction of cell death by Doxorubicin in **multicellular** spheroids as studied by confocal laser scanning microscopy.

AU Wartenberg M; Acker H

CS Max-Planck-Institut fur Molekulare Physiologie, Dortmund, Germany.

SO ANTICANCER RESEARCH, (1996 Mar-Apr) 16 (2) 573-9.

Journal code: 59L. ISSN: 0250-7005.

CY Greece

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; Cancer Journals

EM 199610

AB In the present study the effects of the anticancer drug Doxorubicin (Dox) on necrosis development and cell lethality of **multicellular** DU-145 spheroids (MCS) were examined. **Multicellular** spheroids consist of a peripheral rim of proliferating cells, a inner shell of nonproliferating, quiescent cells and a central core of dead cells. After the application of Dox for different time periods dead cell areas and single dead cells in MCS of different size classes were identified using a set of lethal fluorescence dyes, and a confocal laser scanning microscope (CLSM). The distribution of Dox within MCS was examined by determining Dox fluorescence in single cells and cell areas. Outgrowth experiments were performed to show the effects of Dox on cancer cell migration and cell proliferation. The application of low (400 nM) concentrations of Dox over a time period of 2hours resulted in distinct Dox fluorescence staining of the most peripheral cell layers of the MCS. After long term incubation (48hours) cell lethality was most prominent in large spheroids (diameter between 350 and 800 micron) which possess a dead cell core and single dead cells at the periphery. These MCS showed an approximately 120 microm +/- 30 microm increased dead cell core as compared to control MCS. The cytotoxic effect of Dox was lower in MCS of a diameter between 150-350 microm and nearly no cytotoxic effects were found in spheroids smaller than 150 microm in diameter. Dox fluorescence persisted in dead cells for at least three days. During this time the cytotoxic agent leaked slowly from dead cells and penetrated into the layers of quiescent cells and proliferating cells mediating a prolonged cytotoxicity. In conclusion, the most efficient cytotoxic effect on MCS larger than 150 microm in diameter, can be achieved using a Dox concentration of 400 nM, and applying the drug for long incubation periods to allow its accumulation and storage in the dead cell core and in the single dead cells within vital cell layers. Dox is gradually delivered from these storage sites and kills proliferating and quiescent cells when no Dox is present in the external medium.

CT Check Tags: Human; Male; Support, Non-U.S. Gov't

*Antibiotics, Anthracycline: PD, pharmacology
Cell Death

*Doxorubicin: PD, pharmacology

Drug Screening Assays, Antitumor
 Microscopy, Confocal
 Necrosis
 Prostatic Neoplasms: DT, drug therapy
 Prostatic Neoplasms: PA, pathology
 *Spheroids: DE, drug effects
 Spheroids: PA, pathology
 Tumor Cells, Cultured

L22 ANSWER 7 OF 27 MEDLINE
 AN 96091058 MEDLINE
 DN 96091058
 TI Antiproliferative potential of cytostatic drugs on neuroblastoma cells in vitro. 41/1
 AU Fulda S; Honer M; Menke-Moellers I; Berthold F
 CS Department of Pediatric Hematology and Oncology, Children's Hospital, University of Cologne, Germany.
 SO EUROPEAN JOURNAL OF CANCER, (1995) 31A (4) 616-21.
 Journal code: ARV. ISSN: 0959-8049.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; Cancer Journals
 EM 199602
 AB The role of single drugs in the treatment of neuroblastoma is poorly defined. We, therefore, tested neuroblastoma cell survival after a 72 h exposure to one of 19 cytostatic drugs by **monolayer** proliferation assay. 6 cell lines (IMR-5, Kelly, SK-N-SH, GI-CA-N, CHP-100, CHP-134) were selected on the basis of MYCN amplification and PGY1 overexpression. ED50 drug concentrations were related to plasma levels achievable in patients during chemotherapy. More effective substances were mitoxantrone, doxorubicin, hydroxyurea, bleomycin, dactinomycin, cisplatinum, thiotepa, melphalan, carboplatinum, etoposide, vincristine, cytarabine, 6-thioguanine, cyclophosphamide, ifosfamide and zilascorb. Parental drugs (cyclophosphamide, cisplatinum) appeared more cytotoxic on a molar basis than derived drugs (ifosfamide, carboplatinum). Less effective drugs included 5-fluorouracil, 6-mercaptopurine, CCNU and procarbazine. Fractional application of a given dose was more efficient than a single dose of cyclophosphamide, ifosfamide and cisplatinum. The tested neuroblastoma cell lines showed distinct sensitivities to cytostatic drugs. Cell lines with MYCN amplification appeared more sensitive than PGY1 overexpressing cells. In conclusion, comparative in vitro testing of cytostatic drugs may provide a rationale for their clinical evaluation. Investigation of drug combinations and application of the **monolayer** proliferation assay to tumour biopsy material for preclinical chemosensitivity testing are clearly warranted.
 CT Check Tags: Human; Support, Non-U.S. Gov't
 Antineoplastic Agents: BL, blood
 *Antineoplastic Agents: PD, pharmacology
 Cell Division: DE, drug effects
 Dose-Response Relationship, Drug
 *Drug Screening Assays, Antitumor: MT, methods
 Neuroblastoma: BL, blood
 Neuroblastoma: DT, drug therapy
 *Neuroblastoma: PA, pathology

Tumor Cells, Cultured: DE, drug effects

L22 ANSWER 8 OF 27 MEDLINE
 AN 95329218 MEDLINE
 DN 95329218
 TI Contribution of O6-methylguanine-DNA methyltransferase to monofunctional alkylating-agent resistance in human brain tumor-derived cell lines.
 AU Bobola M S; Blank A; Berger M S; Silber J R
 CS Department of Neurological Surgery, University of Washington, Seattle 98195, USA.
 NC T32CA-09437 (NCI)
 OIG-R35-CA39903 (NCI)
 SO MOLECULAR CARCINOGENESIS, (1995 Jun) 13 (2) 70-80.
 Journal code: AEQ. ISSN: 0899-1987.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; Cancer Journals
 EM 199510
 AB The DNA repair protein O6-methylguanine-DNA methyltransferase (MGMT) has been implicated in resistance of human brain tumors to alkylating agents. We observed that 14 human medulloblastoma- and glioma-derived cell lines differ in sensitivity to the methylating agent N-methyl-N'-nitro-N-nitrosoguanidine (MNNG), as shown by their 28-fold range in 10% survival dose (LD10). By using the substrate analogue inhibitor O6-benzylguanine (O6-BG), we showed that the contribution of MGMT to resistance varies widely, as evidenced by 3- to 30-fold reductions in LD10 among the lines, and varies up to 20-fold among subpopulations of individual lines. Importantly, variability in resistance, manifested as a 20-fold range in LD10, persists after measurable MGMT is eliminated, disclosing differential contributions of other resistance mechanisms to survival. Cells exposed to MNNG while suspended in growth medium are more resistant than cells alkylated as subconfluent **monolayers**, and MGMT accounts for a smaller proportion of their resistance. Notably, the MGMT content of the lines is not statistically correlated with MNNG resistance or with potentiation of killing by O6-BG, even though MGMT is a biochemically demonstrated determinant of resistance. In contrast, the same lines vary less in resistance to the ethylating agent N-ethylnitrosourea (ENU), and MGMT makes only a small contribution to resistance. Our results strongly indicate that resistance to both MNNG and ENU is multifactorial.
 CT Check Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
 Alkylating Agents: PD, pharmacology
 *Alkylating Agents: TO, toxicity
Antineoplastic Agents: PD, pharmacology
 *Brain Neoplasms: DT, drug therapy
 *Brain Neoplasms: EN, enzymology
 Cell Adhesion: PH, physiology
 Colonic Neoplasms: DT, drug therapy
 Colonic Neoplasms: EN, enzymology
 Culture Media
 Drug Resistance
Drug Screening Assays, Antitumor
 *Ethylnitrosourea: TO, toxicity

*Glioma: DT, drug therapy
 *Glioma: EN, enzymology
 *Medulloblastoma: DT, drug therapy
 *Medulloblastoma: EN, enzymology
 Methylation
 *Methylnitrosoguanidine: TO, toxicity
 *Methyltransferases: PH, physiology
 Tumor Cells, Cultured: DE, drug effects

L22 ANSWER 9 OF 27 MEDLINE
 AN 95012880 MEDLINE
 DN 95012880
 TI Resistance to verapamil sensitization of multidrug-resistant cells grown as **multicellular** spheroids.
 AU Sakata K; Kwok T T; Gordon G R; Waleh N S; Sutherland R M
 CS Department of Cell and Molecular Biology, SRI International, Menlo Park, CA 94025-3493.
 NC CA 37618 (NCI)
 CA 20329 (NCI)
 SO INTERNATIONAL JOURNAL OF CANCER, (1994 Oct 15) 59 (2) 282-6.
 Journal code: GQU. ISSN: 0020-7136.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; Cancer Journals
 EM 199501
 AB The ability of verapamil to overcome resistance to adriamycin in a multidrug-resistant derivative of the V79 cell line (LZ), grown as **multicellular** spheroids or as **monolayers**, was examined. Verapamil was much less effective in overcoming resistance to adriamycin in spheroids than in **monolayers**. Verapamil increased the adriamycin content of cells grown as **monolayers**, but had no significant effect on the drug content of spheroids. This occurred in spite of the same *mdr-I* mRNA and protein levels in **monolayers** and spheroids. When the surviving fraction of cells was normalized to the cellular adriamycin content, cells both in **monolayers** and spheroids treated with verapamil were still more sensitive to adriamycin than their counterparts not treated with verapamil. The observed resistance of spheroids to adriamycin and verapamil sensitization may be caused by a drug-resistance mechanism that is functional only in spheroids, in addition to the activity of P-glycoprotein. **Multicellular** tissue architecture and cell-cell contact may play significant roles in this type of multidrug-resistance mechanism.
 CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
 Cell Division: DE, drug effects
 Cricetulus
 Doxorubicin: PK, pharmacokinetics
 Doxorubicin: TO, toxicity
 *Drug Resistance, Multiple
 Drug Screening Assays, Antitumor
 Hamsters
 Models, Biological
 *Tumor Cells, Cultured: DE, drug effects
 *Verapamil: PD, pharmacology

4/1

L22 ANSWER 10 OF 27 MEDLINE
 AN 95007961 MEDLINE
 DN 95007961
 TI The three-dimensional question: can clinically relevant tumor drug resistance be measured in vitro?
 AU Hoffman R M
 CS AntiCancer, Inc., San Diego, CA 92111.
 SO CANCER AND METASTASIS REVIEWS, (1994 Jun) 13 (2) 169-73. Ref: 26
 Journal code: C9H. ISSN: 0891-9992.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA English
 FS Priority Journals
 EM 199501
 AB In vivo-like drug responses are observed in three-dimensional culture but frequently not in two-dimensional culture, indicating that drug response may be a function of tissue architecture. Alexis Carrel introduced that in vitro culture of tissues in the beginning of the century utilizing a culture system that allowed the three-dimensional growth of tissues. Leighton improved upon this system by developing a substrate of sponge matrices. Other methods of three-dimensional culture include collagen gels and what are known as organ culture systems on filters or meshes. In addition, cell suspensions can be converted into **multicellular** spheroids, another form of three-dimensional culture. Comparison of the three-dimensional culture methods with two-dimensional culture methods has shown critical differences in drug response. The in vivo mechanism of drug resistance may involve alterations in cell-cell interaction which may occur in three-dimensional culture as opposed to **monolayer** culture.

CT Check Tags: Animal; Comparative Study
 ***Antineoplastic Agents: PD, pharmacology**
 *Drug Resistance
 ***Drug Screening Assays, Antitumor: MT, methods**
 *Neoplasms, Experimental: DT, drug therapy
 *Neoplasms, Experimental: PA, pathology
Tumor Cells, Cultured: DE, drug effects

L22 ANSWER 11 OF 27 MEDLINE
 AN 94251878 MEDLINE
 DN 94251878
 TI Inhibition of P-glycoprotein-mediated vinblastine transport across HCT-8 intestinal carcinoma **monolayers** by verapamil, cyclosporine A and SDZ PSC 833 in dependence on extracellular pH.
 AU Zacherl J; Hamilton G; Thalhammer T; Riegler M; Cosentini E P; Ellinger A; Bischof G; Schweitzer M; Teleky B; Koperna T; et al
 CS I. Department of Surgery, University of Vienna, Austria.
 SO CANCER CHEMOTHERAPY AND PHARMACOLOGY, (1994) 34 (2) 125-32.
 Journal code: C9S. ISSN: 0344-5704.
 CY GERMANY: Germany, Federal Republic of
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; Cancer Journals
 EM 199409
 AB The ability of the multidrug resistance modifiers R- and

R,S-verapamil (VPL), cyclosporine A (CsA) and its non-immunosuppressive derivative SDZ PSC 833 (PSC 833) to inhibit P-glycoprotein (P-gp)-mediated transepithelial flux of tritiated vinblastine was investigated using tight and highly resistant ($R > 1,400$ omega cm²) **monolayer** cultures of intestinal adenocarcinoma-derived HCT-8 cells grown on permeable tissue-culture inserts. Apical addition of these chemosensitizers inhibited drug flux (137 pmol h⁻¹ cm⁻²; range, 133-142 pmol h⁻¹ cm⁻²) in the basal to apical secretory direction at clinically relevant concentrations, with PSC 833 showing the highest activity, exhibiting inhibition at concentrations as low as 10 ng/ml (9 nM). Acidification of the modulator-containing apical compartment to an extracellular pH (pH_o) of 6.8 had no influence on MDR reversal by CsA at 1 microgram/ml (0.9 microM; flux inhibition, 52%) or by PSC 833 at 100 ng/ml (0.09 microM; flux inhibition, 60%), in contrast to R,S- and R-VPL, which showed decreased inhibition and caused less accumulation of vinblastine in HCT-8 cells under this condition (flux inhibition of 35% and 23%, respectively, at pH_o 6.8 vs 50% and 43%, respectively, at pH_o 7.5). P-gp-mediated rhodamine 123 efflux from dye-loaded single-cell suspensions of HCT-8 cells as measured by flow cytometry was not impeded at pH_o 6.8 in comparison with pH_o 7.5 in standard medium, but at low pH_o the inhibitory activity of R-VPL (29% vs 60% rhodamine 123 efflux inhibition) was diminished significantly, again without a reduction in the effect of PSC 833 (rhodamine 123 flux inhibition, 75%). In conclusion, drug extrusion across polarised **monolayers**, which offer a relevant model for normal epithelia and tumour border areas, is inhibited by the apical presence of R,S- and R-VPL, CsA and PSC 833 at similar concentrations described for single-cell suspensions, resulting in increased (2.2- to 3.7-fold) intracellular drug accumulation. Functional apical P-gp expression, the absence of paracellular leakage and modulator-sensitive rhodamine 123 efflux in single HCT-8 cells indicate a P-gp-mediated transcellular efflux in HCT-8 **monolayers**. In addition to its high MDR-reversing capacity, the inhibitory activity of PSC 833 is not affected by acidic extracellular conditions, which reduce the VPL-induced drug retention significantly. As far as MDR contributes to the overall cellular drug resistance of solid tumours with hypoxic and acidic microenvironments, PSC 833 holds the greatest promise for clinical reversal of unresponsiveness to the respective group of chemotherapeutics.

CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't

Adenocarcinoma: DT, drug therapy

*Adenocarcinoma: ME, metabolism

*Antineoplastic Agents, Combined: TU, therapeutic use

Biological Transport: DE, drug effects

*Carrier Proteins: AI, antagonists & inhibitors

Carrier Proteins: DE, drug effects

Carrier Proteins: ME, metabolism

Cyclosporine: AD, administration & dosage

Cyclosporins: AD, administration & dosage

Depression, Chemical

Drug Resistance

Drug Screening Assays, Antitumor

Hydrogen-Ion Concentration

Ileal Neoplasms: DT, drug therapy

*Ileal Neoplasms: ME, metabolism

*Ileocecal Valve
 *Membrane Glycoproteins: AI, antagonists & inhibitors
 Membrane Glycoproteins: DE, drug effects
 Membrane Glycoproteins: ME, metabolism
 *Neoplasm Proteins: AI, antagonists & inhibitors
 Neoplasm Proteins: DE, drug effects
 Neoplasm Proteins: ME, metabolism
Tumor Cells, Cultured: DE, drug effects
Tumor Cells, Cultured: ME, metabolism
 Verapamil: AD, administration & dosage
 *Vinblastine: AI, antagonists & inhibitors
 Vinblastine: PK, pharmacokinetics

L22 ANSWER 12 OF 27 MEDLINE

AN 94167749 MEDLINE

DN 94167749

TI A convenient and inexpensive chemo-radiosensitivity assay for lung cancer cells using **Terasaki's** microplate.

AU Kobayashi S; Okada S; Yoshida H; Hasumi T; Sato N; Inaba H; Nakada T; Fujimura S

CS Department of Surgery, Tohoku University, Sendai..

SO TOHOKU JOURNAL OF EXPERIMENTAL MEDICINE, (1993 Sep) 171 (1) 65-75.
 Journal code: VTF. ISSN: 0040-8727.

CY Japan

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199406

AB We devised a simple in vitro sensitivity test for lung cancer cells using **Terasaki's** microplate. We used the test to screen for sensitivity to various carcinostatic drugs and radiation, and to determine the optimum method of administration. This assay has been used in routine clinical examinations because about 40% of non-small cell carcinoma and 80% of small cell carcinoma of the lung can be subcultured. We describe here our patients who underwent treatment, various sensitivity tests and the preparation of an optimal course of treatment based upon the results of the sensitivity tests. Cells were placed in primary culture as previously described for short-term selective culture, and 2nd-3rd generation subcultured cells were transferred to individual wells of **Terasaki's** microplates for various sensitivity tests. After culture for 10 days, the effect was evaluated using 0.1% iodonitrotetrazolium (INT). This test permits a variety of sensitivity tests and various studies of clinical models of intensive treatment to be performed conveniently and reproducibly, because subcultured cancer cells are used. Another advantage is that these cells can be applied to basic investigations, including the preparation of monoclonal antibodies and chromosomes, DNA ploidy and oncogene studies.

CT Check Tags: Human

*Antineoplastic Agents, Combined: PD, pharmacology
 Cell Division: DE, drug effects
 Combined Modality Therapy

*Drug Screening Assays, Antitumor: IS, instrumentation

*Lung Neoplasms: DT, drug therapy

Lung Neoplasms: PA, pathology

Lung Neoplasms: RT, radiotherapy

*Radiation Tolerance

Tomography, X-Ray Computed

4/1

L22 ANSWER 13 OF 27 MEDLINE
 AN 94001063 MEDLINE
 DN 94001063
 TI In vitro prediction of cytostatic drug resistance in primary cell cultures of solid malignant tumours.
 AU Dietel M; Bals U; Schaefer B; Herzig I; Arps H; Zabel M
 CS Institute of Pathology, Christian-Albrechts-Universitat zu Kiel, F.R.G.
 SO EUROPEAN JOURNAL OF CANCER, (1993) 29A (3) 416-20.
 Journal code: ARV. ISSN: 0959-8049.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; Cancer Journals
 EM 199401
 AB The in vitro **monolayer** proliferation assay (MP-assay) described here enables predictive determination of the efficacy of anticancer drugs considered for clinical application. The assay was designed (1) to achieve a high plating efficiency, (2) to adapt in vitro growth as close as possible to in vivo conditions, and (3) to prove that the cells in vitro correspond with the in vivo tumour cells they were derived from. From 452 freshly explanted or biopsied tumours, 321 (71%) proliferating cultures could be established. To prove malignant origin of the incubated cells each strain was characterised by DNA-cytophotometry for aneuploidy and by immunocytochemistry for marker proteins. Drug potency was determined by comparing the number of living cells in drug-treated cultures with non-treated controls. Drug concentrations in vitro corresponded with those achievable in tumour tissue and thus represented clinically relevant levels. Growth inhibition in vitro was correlated with in vivo tumour response. Two hundred in vitro/in vivo correlations were performed (50 retrospective, 150 prospective). Overall predictive accuracy of the MP-assay was 86%, with correct indication of resistance in 94.5% and of sensitivity in 75.8% ($P < 0.001$). The results show that the proposed assay is capable of estimating the response probability of cytostatic drugs in individual tumours and thus can contribute to reducing the applications of non-effective drugs and, within limitations, to improving the basis of drug selection.
 CT Check Tags: Human; Support, Non-U.S. Gov't
***Antineoplastic Agents: PD, pharmacology**
 Dose-Response Relationship, Drug
 Drug Resistance
Drug Screening Assays, Antitumor
 Mitosis: DE, drug effects
 Predictive Value of Tests
***Tumor Cells, Cultured: DE, drug effects**

L22 ANSWER 14 OF 27 MEDLINE
 AN 93310904 MEDLINE
 DN 93310904
 TI Characterization and the clinical application of cultured human pulmonary carcinoma cells.
 AU Kobayashi S; Fujimura S
 CS Department of Surgery, Tohoku University, Sendai, Japan.

SO TOHOKU JOURNAL OF EXPERIMENTAL MEDICINE, (1992 Oct) 168 (2) 375-86.
Journal code: VTF. ISSN: 0040-8727.

CY Japan

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199310

AB We had developed a new method for the selective cultivation of cancer cells in short-term. As a result of these improvement in the culture technique, long-term subcultures of cancer cells are possible in about 80% of cases of small cell carcinoma of the lung and nearly 40% of cases of non-small cell carcinoma of the lung. 23 small cell lung carcinoma (SCLC) cell lines, 48 non-SCLC cell lines and 4 metastatic lung tumor cell lines were established in our institute using the culture method. Fractional culture of cells exhibiting the same growth pattern in primary culture produce several subtype cell lines, which can be used in experimental studies of the heterogeneity of lung cancer and in treatment of patients with lung cancer. Using subcultured cancer cells of the second or third generation, we have developed and have clinically utilized a simple sensitivity test with a Terasaki's microplate for anticancer drugs. In 15 surgical patients with SCLC treated between April 1982 and March 1985, the sensitivity test was used to select optimal anticancer drugs for postoperative chemotherapy. The routine use of the sensitivity test in selecting postoperative chemotherapy definitely improved the 3-year survival rate from 38% to 52%.

CT Check Tags: Human
*Drug Screening Assays, Antitumor
*Lung Neoplasms: PA, pathology
Lung Neoplasms: TH, therapy
Tumor Cells, Cultured

L22 ANSWER 15 OF 27 MEDLINE

AN 93304898 MEDLINE

DN 93304898

TI A newly developed hexamethylmelamine derivative, SAE9 with both antitumor and aromatase-inhibitory activity.

AU Tanino H; Kubota T; Yamada Y; Koh J I; Takeuchi T; Kase S; Furukawa T; Takahashi M; Fukuda S; Ogose N; et al

CS Department of Surgery, School of Medicine, Keio University, Tokyo, Japan.

SO ANTICANCER RESEARCH, (1993 May-Jun) 13 (3) 623-6.
Journal code: 59L. ISSN: 0250-7005.

CY Greece

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; Cancer Journals

EM 199309

AB Hexamethylmelamine (HMM) has previously been shown to be active against ovarian, breast and small cell lung cancer. However HMM dose not have aromatase-inhibitory activity. A newly developed HMM derivative, 2-N,N-dimethylamino-4, 6-bis (1-H-imidazol-1-yl)-1,3,5-triazine (SAE9), was found to have direct antitumor activity as well as aromatase-inhibitory activity. The direct antitumor activity on breast carcinoma cell lines (MCF-7, R-27 and MDA-MB-231) was assessed using the 3-(4,5-dimethylthiazol-2yl)-2, 5-diphenyl

tetrazolium bromide (MTT) on cells growing in **monolayer** culture. The 50% inhibitory concentrations (IC50) of SAE9 were found to be approximately 10^{-4} M for each cell line, roughly equivalent to those of HMM. When the aromatase-inhibitory effect was assessed using a human placental aromatase-inhibitory assay, the IC50 of SAE9 was 5.5×10^{-7} M, which was superior to that of aminoglutethimide (AG) (3.8×10^{-5} M). In a rat uterine growth model treated with androstenedione as the in vivo aromatase inhibition assay, SAE9 had an effect equivalent to that of AG. Since SAE9 has both antitumor and aromatase-inhibitory activity on breast carcinoma cell lines with estrogen dependency, this and similar non-steroidal aromatase inhibitors are thought to be promising for further study.

CT Check Tags: Animal; Female; Human
 *Altretamine: AA, analogs & derivatives
 Altretamine: PD, pharmacology
 Aminoglutethimide: PD, pharmacology
 *Aromatase: AI, antagonists & inhibitors
 *Breast Neoplasms: DT, drug therapy
 Drug Screening Assays, Antitumor
 Rats
 Rats, Wistar
 Swine
 Tumor Cells, Cultured: DE, drug effects

L22 ANSWER 16 OF 27 MEDLINE
 AN 93258594 MEDLINE
 DN 93258594
 TI A new in vivo assay of the reactions of microencapsulated human tumor cells to chemotherapeutic drugs.
 AU Hwang J M; Chen C F; Hsu W L; Chen K Y
 CS Department of Radiation Oncology, Tri-Service General Hospital, Taipei, Taiwan, R.O.C.
 SO CHUNG-HUA I HSUEH TSA CHIH [CHINESE MEDICAL JOURNAL], (1993 Mar) 51 (3) 166-75.
 Journal code: CHQ. ISSN: 0578-1337.
 CY TAIWAN: Taiwan, Province of China
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 EM 199308
 AB A new cell culture modality had already been established in our laboratory. Using this model, living KB and GBM 8401 tumor cells grew and proliferated exponentially in semipermeable microcapsules, implanted in vivo. The culture method was designed as a modality for a predictive anticancer drug sensitivity test. Its advantages included providing a three-dimensional growth and in vivo supply of nutrients. Tumor cell sensitivity to drugs can be assessed in vivo. The assay is applicable to virtually all histological types of human tumor cells. Using this technique, anticancer drug sensitivity tests of KB and GBM 8401 cells were evaluated. The results showed that such encapsulated cells grew and proliferated rapidly. In addition, the proliferation of KB cells was more rapid than that of GBM 8401 cells under conventional **monolayer** and in vivo microcapsule culture states. They were very sensitive to adriamycin and fluorouracil, and relatively resistant to cyclophosphamide while cultured in vitro. The viability percentage of microencapsulated KB cells cultured in vivo for two weeks was around 80-90%, roughly similar to that of the same cells conventionally cultured in vitro.

However, the proliferation rates of encapsulated KB and GBM 8401 cells in vivo were significantly inhibited by all the drugs tested, with KB cells inhibited more significantly than GBM 8401. These results also suggest that some anticancer drugs needing to be bioactivated in vivo had better test results by this technique, and thus false negative results could be excluded. Also, the good repair capacity of microcapsules implanted in vivo, for damaged tumor cells previously incubated with chemotherapeutic drugs, appears to provide a much better environment for cell growth because much essential nourishment can be supplied. The inhibition percentage of fluorouracil to encapsulated cancer cells from patients with adenocarcinoma of the colon was also tested; they were 69.8% in vivo and 76.5% in vitro. This fast, relatively inexpensive in vivo model can be used to screen various anticancer drugs and help clinical oncologists to select the most effective agents for individual patients.

CT Check Tags: Animal; Female; Human; Male
***Antineoplastic Agents: PD, pharmacology**
 Cell Division: DE, drug effects
***Drug Screening Assays, Antitumor**
 KB Cells: DE, drug effects
 Mice
 Mice, Inbred C3H
 Neoplasm Transplantation
 Neoplasms, Experimental: DT, drug therapy
***Tumor Cells, Cultured: DE, drug effects**

L22 ANSWER 17 OF 27 MEDLINE

AN 93251368 MEDLINE

DN 93251368

TI Response of primary colon cancer cells in hybrid spheroids to 5-fluorouracil.

AU Djordjevic B; Lange C S; Allison R R; Rotman M

CS Department of Radiation Oncology, State University of New York, Brooklyn 11203.

SO CANCER INVESTIGATION, (1993) 11 (3) 291-8.

Journal code: CAI. ISSN: 0735-7907.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; Cancer Journals

EM 199308

AB We have measured the clonogenic survival of cells isolated directly from colon cancer surgical specimens and treated with 5-fluorouracil (5-FU). Enzymatically disassociated cells were incorporated into hybrid spheroids, consisting predominantly of nonproliferating HeLa feeder cells. Aliquots were exposed for 1.5 hr to a range of concentrations of 5-FU. From the decrease in clonogenic survival, as deduced from the frequency of colony formers among hybrid spheroids after chemical treatment, we were able to construct survival curves in 50% of the surgical specimens tested. A striking revelation was the presence of a resistant plateau in the survival curves, reminiscent of the solid tumor response to treatment with 5-FU. This resistance was absent in **monolayer** cultures. Evidence is presented that this resistance is due to the absence of, or delay in, cell cycle progression of cells residing in hybrid spheroids.

CT Check Tags: Human; Support, Non-U.S. Gov't

Cell Survival
 *Colonic Neoplasms: DT, drug therapy
 Colonic Neoplasms: PA, pathology
 Drug Resistance
 Drug Screening Assays, Antitumor: MT, methods
 Feasibility Studies
 *Fluorouracil: TU, therapeutic use
 HeLa Cells: DE, drug effects
 Predictive Value of Tests
 Tumor Stem Cell Assay

L22 ANSWER 18 OF 27 MEDLINE
 AN 91321418 MEDLINE
 DN 91321418
 TI Studies of the effects of associated photodynamic therapy and drugs on macromolecular synthesis of tumoral cells grown in vitro.
 AU Dima V F; Mihailescu I N; Dima S V; Chivu L; Stirbet M; Udrea M; Popa A
 CS Cantacuzino Institute, Bucharest, Romania.
 SO ARCHIVES ROUMAINES DE PATHOLOGIE EXPERIMENTALES ET DE MICROBIOLOGIE, (1990 Apr-Jun) 49 (2) 155-75.
 Journal code: 8EM. ISSN: 0004-0037.
 CY Romania
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 EM 199111
 AB HeLa S3 tumoral cells were used as an experimental model for studying the association of photodynamic therapy (PDT) and antitumoral agents. Tumoral **monolayer** cultures were incubated 18 hours at 37 degrees C with Photofrin II, trypsinized and suspended in Eagle medium supplemented with 10% FCS and then treated with antitumoral agents 90 minutes before He-Ne laser exposure. The tumoral cells were exposed to antitumoral agents in the following concentrations (equivalent to ED70): adriamycin (0.0297 micrograms); mitomycin C (0.0199 micrograms); 5-FU (0.4937 micrograms) and vinblastine (0.0109 micrograms) per 10(5) cells. Macromolecular syntheses (DNA, RNA and proteins) were investigated by use of radioactive precursors: 3H-thymidine, 3H-uridine and 3H-leucine, as expressed in percent referring to Photofrin II-pretreated controls; they were exposed to He-Ne laser but not treated with antitumoral agents. All experiments were followed for 72 hours incubation at 37 degrees C. The conclusions of the results of PDT associated with antitumoral agents sustain the following aspects: a) the antitumoral agents activity (adriamycin, mitomycin C, 5-FU, vinblastine) was more noticeable when applied 90 minutes before He-Ne laser irradiation; b) inhibition of radioactive precursors uptake in DNA, RNA and proteins was accompanied by suppression of in vitro tumoral cells development and c) PDT association with antitumoral agents could manifest at least three positive effects upon animals; 1) PDT potentiating effects with antitumoral agents; 2) suppressing effects on tumoral macromolecular synthesis; 3) antitumoral agents cytotoxic elimination (due to the low doses used).
 CT Check Tags: Comparative Study; Female; Human
 *Antineoplastic Agents, Combined: TU, therapeutic use
 *Carcinoma: DT, drug therapy
 Carcinoma: ME, metabolism

Carcinoma: UL, ultrastructure
 Cell Line
 *Cervix Neoplasms: DT, drug therapy
 Cervix Neoplasms: ME, metabolism
 Cervix Neoplasms: UL, ultrastructure
 Doxorubicin: AD, administration & dosage
 Drug Screening Assays, Antitumor
 Hela Cells
 Lasers: TU, therapeutic use
 Macromolecular Systems
 Microscopy, Electron, Scanning
 Mitomycins: AD, administration & dosage
 *Photochemotherapy
 Time Factors
 Tumor Cells, Cultured: DE, drug effects
 Tumor Cells, Cultured: ME, metabolism
 Tumor Cells, Cultured: UL, ultrastructure
 Vinblastine: AD, administration & dosage

L22 ANSWER 19 OF 27 MEDLINE
 AN 91151650 MEDLINE
 DN 91151650
 TI Antiproliferative effects of cytokines on squamous cell carcinoma.
 AU Sacchi M; Klapan I; Johnson J T; Whiteside T L
 CS Department of Otolaryngology, University of Pittsburgh School of
 Medicine, PA.
 SO ARCHIVES OF OTOLARYNGOLOGY -- HEAD AND NECK SURGERY, (1991 Mar) 117
 (3) 321-6.
 Journal code: ALQ. ISSN: 0886-4470.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 199106
 AB A panel of 12 squamous cell carcinoma of the head and neck (SCCHN)
 cell lines has been used to determine sensitivity of tumor cells to
 cytokines, tumor necrosis factor alpha (TNF-alpha), interferon gamma
 (IFN-gamma), and interferon alfa (IFN-alpha) in vitro.
 Antiproliferative activity of these cytokines on squamous cell
 carcinoma of the head and neck **monolayers** was measured in
 a colorimetric MTT [3-(4,5-dimethylthiazol-2yl)-2,5-diphenyl
 tetrazolium bromide]-based assay. All 12 cell lines tested were
 sensitive to IFN-gamma, with the 50% inhibitory dose (ID50) ranging
 from 0.07 +/- 0.001 to 104 +/- 4.6 U/mL. The TNF-alpha showed
 antiproliferative activity on three cell lines at relatively high
 doses (ID50 from 55 +/- 4.1 to 847.10 +/- 10 U/mL), and IFN-alpha
 was growth inhibitory in only one line (ID50 = 1211 +/- 46.2 U/mL).
 The combination of IFN-gamma and TNF-alpha had a synergistic
 antiproliferative effect on eight cell lines and an additive effect
 on two cell lines. In two cell lines, the effect of the combination
 was equal to that of IFN-gamma alone. A combination of IFN-alpha and
 TNF-alpha resulted in cell growth inhibition in six of the seven
 lines tested, and this effect was synergistic. These in vitro
 studies indicate that combinations of IFN-gamma and TNF-alpha or
 IFN-alpha and TNF-alpha may be more growth inhibitory against
 squamous cell carcinoma of the head and neck and at lower doses than
 each of these cytokines used singly.

CT Check Tags: Support, Non-U.S. Gov't
 *Carcinoma, Squamous Cell: TH, therapy
 *Cell Division: DE, drug effects
 Cell Line
 *Cytokines: PD, pharmacology
 Cytokines: TU, therapeutic use
 Dose-Response Relationship, Drug
Drug Screening Assays, Antitumor
 *Head and Neck Neoplasms: TH, therapy
 Interferon Alfa, Recombinant: PD, pharmacology
 Interferon Alfa, Recombinant: TU, therapeutic use
 Interferon-gamma, Recombinant: PD, pharmacology
 Interferon-gamma, Recombinant: TU, therapeutic use
 Tumor Cells, Cultured: DE, drug effects
 Tumor Necrosis Factor: PD, pharmacology
 Tumor Necrosis Factor: TU, therapeutic use

L22 ANSWER 20 OF 27 MEDLINE
 AN 91086973 MEDLINE
 DN 91086973
 TI The VM model of glioma: preparation of multicellular
 tumour spheroids (MTS) and their response to chemotherapy.
 AU Bradford R; Darling J L; Sier N; Thomas D G
 CS Gough-Cooper Department of Neurological Surgery, Institute of
 Neurology, Queen Square, London, United Kingdom.
 SO JOURNAL OF NEURO-ONCOLOGY, (1990 Oct) 9 (2) 105-14.
 Journal code: JCP. ISSN: 0167-594X.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199104
 AB A cell line, 497-P(1), derived from the VM spontaneous murine
 astrocytoma has been used to develop an in vitro therapeutic model
 of human glioma. In this study we describe the preparation of MTS
 from this cell line. The in vitro chemosensitivity of 497-P(1) MTS
 has been examined and compared to the sensitivity of the
monolayer culture. BCNU and CCNU both produced growth delay
 in MTS at doses below the ID50 of the **monolayer** culture.
 MTS, however, were considerably more resistant to vincristine and
 procarbazine when compared to the **monolayer** culture.

CT Check Tags: Animal; Support, Non-U.S. Gov't
 Carmustine: TU, therapeutic use
 Cell Division: DE, drug effects
 Disease Models, Animal
 *Drug Screening Assays, Antitumor: MT, methods
 *Glioma: DT, drug therapy
 Lomustine: TU, therapeutic use
 Mice
 Procarbazine: TU, therapeutic use
 *Tumor Cells, Cultured: DE, drug effects
 Vincristine: TU, therapeutic use

L22 ANSWER 21 OF 27 MEDLINE
 AN 91073540 MEDLINE
 DN 91073540
 TI Cultured human bladder tumors for pharmacodynamic studies.

AU Schmittgen T D; Au J L; Wientjes M G; Badalament R A; Drago J R
 CS College of Pharmacy, Ohio State University, Columbus 43210.
 NC RO1 CA 49816 (NCI)
 KO4 CA01497
 SO JOURNAL OF UROLOGY, (1991 Jan) 145 (1) 203-7.
 Journal code: KC7. ISSN: 0022-5347.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
 EM 199103
 AB Human bladder tumor fragments were cultured on collagen gel. In this system, the three dimensional architecture, cell-to-stroma and cell-to-cell interactions, and tumor heterogeneity were maintained. Cell viability and labeling index (LI) were determined by exposure to 3H-thymidine and autoradiography. Of the samples from 20 patients with transitional cell carcinoma, 14 (70%) were successfully cultured and had a mean LI of 32%. In addition, one specimen from a patient with squamous cell carcinoma was cultured and had a LI of 61%. Cultured samples were tested for chemosensitivity using a two hour exposure of mitomycin C in concentrations ranging from one to 50 micrograms./ml. A dose-dependent relationship was demonstrated; LI decreased as mitomycin C concentrations increased. The methodology described provides an alternative to suspension or **monolayer** techniques of culturing human bladder tumors for pharmacological studies.

CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
 *Antineoplastic Agents: PD, pharmacology
 Autoradiography
 *Bladder Neoplasms: DT, drug therapy
 *Carcinoma, Squamous Cell: DT, drug therapy
 *Carcinoma, Transitional Cell: DT, drug therapy
 Dose-Response Relationship, Drug
 Drug Screening Assays, Antitumor: MT, methods
 Mitomycins: PD, pharmacology
 Tumor Cells, Cultured: DE, drug effects

L22 ANSWER 22 OF 27 MEDLINE
 AN 90346453 MEDLINE
 DN 90346453
 TI Characterization of a new model of human prostatic cancer: the **multicellular** tumor spheroid.
 AU Donaldson J T; Tucker J A; Keane T E; Walther P J; Webb K S
 CS Department of Surgery, Duke University School of Medicine, Durham, NC 27710.
 NC CA39690 (NCI)
 SO INTERNATIONAL JOURNAL OF CANCER, (1990 Aug 15) 46 (2) 238-44.
 Journal code: GQU. ISSN: 0020-7136.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; Cancer Journals
 EM 199011
 AB **Multicellular** tumor spheroids (MTS) provide a closer in vitro correlate to in vivo malignancy than do conventional **monolayer** cultures; while simulating many parameters of in vivo growth, MTS systems provide those perquisites (i.e.,

experimental control, economy, expediency) associated with in vitro evaluation of preclinical therapeutic strategies. For these reasons, we exploited the proclivity of the highly metastatic human prostatic carcinoma subline I-LN-PC3-IA to spontaneously assume a spheroid morphology under routine culture conditions. I-LN spheroids demonstrate salient features described in other spheroid systems and exhibit histologic characteristics of human prostate carcinoma. Cells encompassed in the I-LN spheroid format demonstrated functional divergence from their **monolayer** counterparts with respect to immunoreactivity for prostatic acid phosphatase, positional dependence of prostate-restricted p40 antigen expression, and chemotherapeutic drug response. This new in vitro-in vivo transition model of human prostatic carcinoma should provide a valuable in vitro context to expediently evaluate in vivo correlates of oncolytic protocols on a malignancy that remains refractive to therapy.

CT Check Tags: Comparative Study; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Antineoplastic Agents: TU, therapeutic use

Cell Line

Cell Separation

Drug Screening Assays, Antitumor

Flow Cytometry

Immunoenzyme Techniques

Microscopy, Electron

*Models, Biological

Oxidation-Reduction

Prostate: PA, pathology

Prostatic Neoplasms: DT, drug therapy

Prostatic Neoplasms: ME, metabolism

*Prostatic Neoplasms: PA, pathology

Thymidine: ME, metabolism

Tumor Cells, Cultured: DE, drug effects

Tumor Cells, Cultured: ME, metabolism

Tumor Cells, Cultured: PA, pathology

L22 ANSWER 23 OF 27 MEDLINE

AN 90314344 MEDLINE

DN 90314344

TI Effectiveness of cis-platin and carboplatin in the chemotherapy of squamous cell carcinoma grown as **multicellular** spheroids.

AU Schwachofer J H; Crooijmans R P; Hoogenhout J; Kal H B; Theeuwes A G

CS Department of Radiotherapy, University Hospital Nijmegen, The Netherlands.

SO ANTICANCER RESEARCH, (1990 May-Jun) 10 (3) 805-11.

Journal code: 59L. ISSN: 0250-7005.

CY Greece

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; Cancer Journals

EM 199010

AB We compared cis-platin (DDP) and its analogue, carboplatin (JM8, CBDCA) in their ability to inhibit spheroid growth. The activities of DDP and JM8 were also compared in an antimetabolic assay for their ability to inhibit (3H)-thymidine incorporation in **multicellular** tumor spheroids. The spheroids were derived from a squamous cell carcinoma cell line HN-1, originally derived

from a tumor of the tongue. To produce equal levels of growth delay in spheroids, carboplatin was required at concentrations approximately 16 times that of DDP. Carboplatin also required much longer incubation periods than DDP to produce equivalent growth delay and proportions of cured spheroids. Reflecting the initial response to chemotherapy, the antimetabolic assay showed that carboplatin was required at higher concentrations and longer exposure times to produce equal inhibition of the nucleotide precursor thymidine. These findings may have implications for the clinical use of these drugs and in particular would support a role for carboplatin in the treatment of squamous cell carcinoma of the head and neck, since total free-drug exposure of patients to carboplatin may be up to 16-fold greater than with DDP, and the clinical side effects of carboplatin have been shown to be well tolerated. However, one must be cautious about applying in vitro data to clinical situations.

CT Check Tags: Human; Support, Non-U.S. Gov't
 *Antineoplastic Agents: PD, pharmacology
 Carcinoma, Squamous Cell
 Cell Division: DE, drug effects
 Cell Line
 Cell Survival: DE, drug effects
 *Cisplatin: PD, pharmacology
Drug Screening Assays, Antitumor
 DNA Replication: DE, drug effects
 *Organoplatinum Compounds: PD, pharmacology
 Thymidine: ME, metabolism
 Tongue Neoplasms
 Tritium
Tumor Cells, Cultured: CY, cytology
***Tumor Cells, Cultured: DE, drug effects**

L22 ANSWER 24 OF 27 MEDLINE

AN 89168162 MEDLINE

DN 89168162

TI Sensitivities of **monolayers** and spheroids of the human bladder cancer cell line MGH-U1 to the drugs used for intravesical chemotherapy.

AU Knuchel R; Hofstadter F; Jenkins W E; Masters J R

CS Department of Pathology, RWTH, Aachen, West Germany.

SO CANCER RESEARCH, (1989 Mar 15) 49 (6) 1397-401.

Journal code: CNF. ISSN: 0008-5472.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; Cancer Journals

EM 198907

AB The in vitro cytotoxicities of the four drugs most frequently used for intravesical chemotherapy (Adriamycin, epodyl, mitomycin C, Thiotepa) and epirubicin were compared using **monolayers** and **multicellular** tumor spheroids of the human bladder cancer cell line, MGH-U1. Adriamycin and epirubicin were most cytotoxic against **monolayer** cultures, whereas mitomycin C killed more cells in spheroids. Epodyl was least cytotoxic against both two- and three-dimensional cultures. Thiotepa was the only drug more cytotoxic to three- than two-dimensional cultures. Topographic analysis of bromodeoxyuridine-stained nuclei using image analysis

indicated that Adriamycin selectively removed or killed superficial cells in **multicellular** tumor spheroids, but had little effect on DNA synthesis within the spheroids. In contrast Thiotepa killed cells throughout the spheroids. These in vitro data appear to reflect clinical experience using intravesical chemotherapy to treat superficial bladder cancer.

CT Check Tags: Human; Support, Non-U.S. Gov't
Administration, Topical
Bladder Neoplasms: DT, drug therapy
*Bladder Neoplasms: PA, pathology
Bromodeoxyuridine: ME, metabolism
Carcinoma, Transitional Cell: DT, drug therapy
*Carcinoma, Transitional Cell: PA, pathology
Cell Survival: DE, drug effects
Doxorubicin: PD, pharmacology
Drug Screening Assays, Antitumor
DNA, Neoplasm: BI, biosynthesis
Thiotepa: PD, pharmacology
*Tumor Cells, Cultured: DE, drug effects

L22 ANSWER 25 OF 27 MEDLINE

AN 88184902 MEDLINE

DN 88184902

TI [Optimization of the growth capacity of cell explants from carcinomas of the mouth in an anti-oncogram. A contribution toward the planning of cytostatic chemotherapy].
Optimierung der Wachstumsfähigkeit von Zellexplantaten aus Mundhöhlenkarzinomen im Antionkogramm. Ein Beitrag zur Planung einer zytostatischen Chemotherapie.

AU Metelmann H R; Sanger E; Dreweck C; Schlesinger S; Bier J

SO DEUTSCHE ZEITSCHRIFT FÜR MUND-, KIEFER-, UND GESICHTS-CHIRURGIE, (1986 Sep-Oct) 10 (5) 345-53.

Journal code: DEU. ISSN: 0343-3137.

CY GERMANY, WEST: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

LA German

FS Dental Journals; Dental

EM 198807

CT Check Tags: Human

*Carcinoma: DT, drug therapy

Drug Screening Assays, Antitumor: IS, instrumentation

*Drug Screening Assays, Antitumor: MT, methods

English Abstract

*Mouth Neoplasms: DT, drug therapy

*Patient Care Planning

Tumor Cells, Cultured

L22 ANSWER 26 OF 27 MEDLINE

AN 88107063 MEDLINE

DN 88107063

TI Effects of cisplatin plus fluorouracil vs cisplatin plus cytarabine on head and neck squamous **multicellular** tumor spheroids.

AU Kohno N; Ohnuma T; Biller H F; Holland J F

CS Department of Neoplastic Diseases, Mount Sinai School of Medicine, New York, NY 10029.

NC CA-15936 (NCI)

SO ARCHIVES OF OTOLARYNGOLOGY -- HEAD AND NECK SURGERY, (1988 Feb) 114

(2) 157-61.
 Journal code: ALQ. ISSN: 0886-4470.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 198805
 AB We compared the efficacy of cisplatin plus fluorouracil vs cisplatin plus cytarabine against HEp-2 head and neck carcinoma cells in **monolayer** and **multicellular** tumor spheroid (MTS) systems. Increases in exposure time to cisplatin and fluorouracil from one to 24 hours resulted in approximately tenfold and 1000-fold increases, respectively, in cell lethality for both **monolayer** and MTS cells. Dose-response curves for cisplatin or fluorouracil on MTS cells closely followed those from **monolayer** cells, indicating good drug penetration into the MTS core. In contrast, dose-response curves on MTS cells after 24-hour exposure to cisplatin and cytarabine showed progressively lesser efficacy at higher drug concentrations. For **monolayer** cells, cisplatin plus fluorouracil and cisplatin plus cytarabine were both synergistic, the latter combination more synergistic than the former. For MTS cells, both combinations again showed synergistic interaction at moderate to high effect levels. Heightened synergistic interaction was demonstrated especially with the cisplatin plus cytarabine combination. Thus, the cisplatin plus cytarabine combination was always more synergistic than cisplatin plus fluorouracil. These data may serve as a basis for additional clinical trials of cisplatin plus cytarabine in the treatment of patients with head and neck carcinoma.
 CT Check Tags: Comparative Study; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
 *Antineoplastic Agents, Combined: TU, therapeutic use
 *Carcinoma, Squamous Cell: DT, drug therapy
 Cell Survival: DE, drug effects
 *Cisplatin: AD, administration & dosage
 *Cytarabine: AD, administration & dosage
 Dose-Response Relationship, Drug
 Drug Screening Assays, Antitumor
 *Fluorouracil: AD, administration & dosage
 *Head and Neck Neoplasms: DT, drug therapy
 Tumor Cells, Cultured: DE, drug effects
 L22 ANSWER 27 OF 27 MEDLINE
 AN 88027477 MEDLINE
 DN 88027477
 TI A comparison of adriamycin and mAMSa. II. Studies with V79 and human tumour **multicellular** spheroids.
 AU West C M; Stratford I J
 CS Paterson Institute for Cancer Research, Christie Hospital and Holt Radium Institute, Manchester, UK.
 SO CANCER CHEMOTHERAPY AND PHARMACOLOGY, (1987) 20 (2) 109-14.
 Journal code: C9S. ISSN: 0344-5704.
 CY GERMANY, WEST: Germany, Federal Republic of
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; Cancer Journals
 EM 198802

- AB **Multicellular** spheroids were used to compare the two chemotherapeutic agents adriamycin (ADM) and 4'[(9-acridinyl)-amino]methanesulphon-m-anisidide (mAMSA). Chinese hamster cells, V79 379A, a human small cell lung carcinoma, designated ME/MAR, and a human melanoma xenograft, HX117, were grown as spheroids (200 or 400 micron in diameter) and treated with either drug for 1 h, at 37 degrees C, in air. Cytotoxicity was assayed using both cell survival and growth delay. Both drugs were highly toxic towards V79 but showed less activity toward the human tumour single cell suspensions; ADM was more effective towards HX117 and ME/MAR than mAMSA. When grown as spheroids, the cells developed marked resistance to both drugs. In all cases, cytotoxicity was drug dose and spheroid size dependent. The response of HX117 spheroids to both drugs was similar. In contrast, ADM was more effective toward 200 micron diameter ME/MAR spheroids, and mAMSA showed greater activity than ADM against V79 spheroids. Both endpoints gave qualitatively equivalent results, and a comparison of the two showed relatively long growth delays for a given level of cell kill, for both drugs and with all three cell lines. The greater cytotoxicity of ADM toward ME/MAR spheroids is consistent with the clinical finding that ADM has a use in the treatment of small cell carcinoma of the lung, while mAMSA has not demonstrated any activity in the treatment of lung cancer.
- CT Check Tags: Animal; Comparative Study; Human; Support, Non-U.S. Gov't
- *Amsacrine: PD, pharmacology
 - Carcinoma, Small Cell
 - Cell Survival: DE, drug effects
 - Cricetulus
 - Dose-Response Relationship, Drug
 - *Doxorubicin: PD, pharmacology
 - Drug Screening Assays, Antitumor**
 - Hamsters
 - Lung Neoplasms: PA, pathology
 - Melanoma: PA, pathology
 - *Tumor Cells, Cultured: DE, drug effects
 - Tumor Cells, Cultured: PA, pathology